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CHOLECYSTITIS AND CYSTIC DUCT OBSTRUCTION

SIGNIFICANCE IN THE FORMATION OF GALLSTONES RICH IN CALCIUM CARBONATE AND IN CALCIFICATION OF THE GALLBLADDER WALL: PRELIMINARY REPORT *

D. B. PHEMISTER, M.D.
ALLAN G. REWBRIDGE, M.D.
AND
HILLYER RUDISILL, M.D.
CHICAGO

Large gallstones in man consisting of a high percentage of calcium carbonate have been but rarely reported and no associated factors have been mentioned as specifically influencing their formation. In a study of seven cases diagnosed as such, the observation was made that in every case the cystic duct was obstructed by a cholesterol-bile pigment, or cholesterol stone, indicating that the duct obstruction was a precursor to and a determining factor in calcium carbonate stone formation in the gallbladder.

Following this obstruction the calcium carbonate was thrown out in large quantities, forming either a separate stone or a mold of the gallbladder which incorporated preexisting cholesterol-bile-pigment stones. A thick mucinous suspension of calcium carbonate may be found which has been described as "calcium milk bile" by Volkmann.[1] In some instances the deposit of calcium carbonate produced the roentgenographic appearance of very markedly concentrated tetiothalein sodium N. N. R. in a gallbladder that was either free from stones or contained radiotranslucent stones. In other cases there was in addition a deposit of calcium carbonate on the gallbladder side of the stone obstructing the cystic duct, thereby making it possible to diagnose the presence of duct obstruction as well by means of the roentgenogram. Four cases have been encountered among 235 cases of gallstones at the University of Chicago Clinics during the past three years and eight months. Three cases are from the outside. The first two cases are reported in full as illustrative of the condition, and the other five are summarized:

CASE 1.—A woman, aged 44, had had repeated attacks of pain in the epigastrium and (curiously) left upper quadrant, extending to the left scapular region for the past fifteen years. Following an attack, cholecystography was performed, March 28, 1928. The roentgenogram taken before the dye was given showed a quarter moon shaped dense shadow in the gallbladder region (fig. 1). There was no change in density in the gallbladder region in the pictures taken after the dye was administered. A second roentgenogram taken seventeen days later showed a shadow of the same size which had taken on a serpentine configuration. In June, 1928, an abdominal hysterectomy was performed for fibroids, at which time palpation revealed a stone in the cystic duct. Following a moderately severe attack of colic another roentgenogram was taken, May 31, 1930. It revealed marked enlargement of the dense shadow in the region of the gallbladder, which had taken on an oval form, and there was a faint half moon shaped shadow in the region of the cystic duct (fig. 2). The patient continued to have slight attacks of colic at irregular intervals. Feb. 28, 1931, a roentgenogram showed slight enlargement of the shadow and a change in contour to that of a half moon. Three days later the shadow had the contour of an agar slant (fig. 3). The shadow in the region of the cystic duct had increased in density. Another roentgenogram, April 27, showed a return of the shadow to approximately the configuration of May 31, 1930.

At operation, April 29, 1931, the gallbladder was found to be moderately contracted and its wall thickened. A stone was found in the gallbladder and one in the cystic duct. Cholecystectomy was performed including the cystic duct containing the stone. A roentgenogram of the specimen (fig. 4) shows a large dense oval shadow in the fundus of the gallbladder, numerous flecks throughout its remaining portion, and an irregular half moon shaped shadow cast by the gallbladder side of the stone in the duct. An attempt at aspiration yielded a small amount of very thick mucus. A longitudinal section of the specimen (fig. 5) showed a cholesterol stone about 0.75 cm. in diameter in the first portion of the duct, with a white deposit on its side projecting into the gallbladder. There was a soft pliable white oval stone in the fundus weighing 4.580 Gm. The rest of the gallbladder was filled by a clear, very thick mucinous material which was dotted irregularly with white flakes. Chemical analysis showed 600 mg. of calcium per hundred cubic centimeters. The wall of the gallbladder was moderately thickened. Aerobic and anaerobic cultures of the mucin and of the wall were negative.

Microscopic sections of the wall revealed moderate fibrous thickening with scattered areas of round cell infiltration. The mucosa was intact in most of its extent but had disappeared over many of the villi, which showed an increase in the number of fibroblasts and round cell infiltration. Some of the villi showed glands markedly distended with mucus.

Chemical analysis of the white stone gave calcium carbonate, 85 per cent, and calcium phosphate, 2.5 per cent. The rest consisted of organic matter. There was no bile pigment or cholesterol.

The second case illustrates the type of calcium carbonate stone which was deposited about other stones forming a cast of the greater extent of the lumen of the gallbladder and giving the roentgenologic picture resembling concentrated tetiothalein sodium:

CASE 2.—A woman, aged 55, had attacks of gallstone colic at irregular intervals for several years. There had never been jaundice but some of the attacks had been accompanied by fever. Physical examination was of no especial interest aside from

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* From the Department of Surgery and the Division of Roentgenology of the University of Chicago.

* Read before the Section on Surgery, General and Abdominal, at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 11, 1931.

1. Volkmann, J.: Ueber kalkmilchartige Galle, München. med. Wchnschr. 73:2014 (Nov. 26) 1926.

tenderness in the right upper quadrant. A roentgenogram (fig. 6) revealed a dense shadow conforming roughly to the outline of the gallbladder but incorporating irregular areas of greatly reduced density suggestive of bile pigment-cholesterol stones. Roentgenograms taken after administration of tetiothalein sodium showed no change in the shadow. At operation March 15, 1927, a thickened gallbladder was found contracted on stones with a stone obstructing the orifice of the cystic duct. Cholecystectomy was performed. On longitudinal section of the gallbladder its wall was found to be slightly thickened. There was a small amount of turbid fluid in the gallbladder that was not bile stained. The rest of the space was occupied by calculi. There was a soft oval white calculus 6 cm. long occupying the central portion. A small white calculus occupied the tip of the fundus and a brown calculus was wedged in the orifice of the cystic duct with a white cap on its gallbladder side. Three small brown pigment stones lay free alongside the large stone. The large soft white stone was found to contain several mottled grayish brown bile pigment-cholesterol stones on the inside.

Fig. 1 (case 1).—Shadow in gallbladder region, April 23, 1928.

Cultures of the fluid in the gallbladder were negative. Microscopic examination of the wall showed moderate thickening with loss of mucous membrane and villi over about nine tenths of the surface lining. At irregular intervals there were small stretches of mucosa and of glands embedded in the deeper tissue. There was moderate fibrosis and round cell infiltration of the wall. Chemical analysis of a portion of the white material comprising the largest stone gave the following results: calcium carbonate, 75 per cent; calcium phosphate, 2 per cent; cholesterol, trace; bile pigment, 0; organic matter the remaining portion.

A summary of the observations in the remaining five cases follows:

Case 3.—A man, aged 65, had had mild attacks of gallstone colic at intervals for seven years. A roentgenogram showed a dense shadow in the gallbladder region of the shape and size of the gallbladder. Cholecystectomy was performed by Dr. E. M. Miller at the Presbyterian Hospital. There was a stone impacted in the cystic duct and a large one in the gallbladder. The gallbladder wall was moderately thickened. The lumen contained a small amount of yellowish green fluid and a grayish oval stone measuring 6.5 by 2.5 cm. with a brown pigment stone incorporated and showing at one end. The stone weighed 18.258 Gm. Chemical analysis of the gray stone revealed calcium carbonate, 80 per cent, calcium phosphate, 0.46 per cent; bilirubin present, and cholesterol absent. Because of the bile stained character of the fluid and interior of the stone there must have been some bile entering the gallbladder past the stone in the cystic duct.

Case 4.—A man, aged 32, had mild attacks of pain in the right upper quadrant at intervals for one year. He was never jaundiced or febrile. A roentgenogram showed a large dense cup-shaped shadow in the region of the fundus of the gallbladder with a smaller ring shaped shadow proximal to it. There was no change in the gallbladder shadow after injection of tetiothalein sodium.

At operation, stones were found in the contracted gallbladder and one in the cystic duct. Cholecystectomy was performed. There was 8 cc. of turbid mucous fluid very slightly bile stained. Chemical analysis of the fluid showed the following: p_H, 7.195; carbon dioxide, 5.55 volumes per cent; calcium, 163 mg. per hundred cubic centimeters; phosphorus, a trace. The gallbladder contained an oval white stone 2.5 by 1.25 cm. with two small bile pigment stones embedded on one side. Chemical analysis of the white material revealed: calcium carbonate, 74 per cent; calcium phosphate, 3.1 per cent; bile pigment and cholesterol, present in traces. There was a smaller cholesterol stone present which showed a calcareous deposit on one side. Cultures from the gallbladder wall yielded anhemolytic streptococci.

Case 5.—A woman, aged 26, had attacks of pain in the right upper quadrant at intervals for two years. A roentgenogram showed a large, somewhat irregular, dense shadow in the gallbladder region. No change occurred in the gallbladder shadow after administration of tetiothalein sodium. Cholecystectomy was performed. There was a stone impacted in the cystic duct near the common duct. The slightly contracted and thickened gallbladder, on being opened, was found to contain a milky white semisolid mass embedded in which were six small white stones. Cultures were negative. A chemical analysis of the white deposit showed it to be composed largely of calcium, but no attempt was made to determine the amounts of carbonate or phosphate present. The white stones were calcium carbonate.

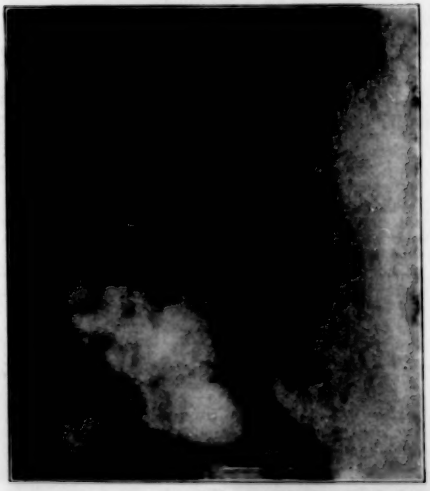


Fig. 2 (case 1).—Shadow in regions of (a) gallbladder and (b) cystic duct, May 31, 1930.

Case 6.—A woman, aged 31, had had attacks of pain in the right upper quadrant for five months. She had no jaundice or fever. Examination showed slight tenderness in the gall-

bladder region. Cholecystography was done and the roentgenogram taken before tetiothalein sodium was given revealed a dense shadow of the outline of the gallbladder and containing

Fig. 3 (case 1).—a, gallbladder shadow and b, cystic duct shadow, March 2, 1931.

numerous negative shadows indicative of small radiotranslucent stones. There was a ring-shaped shadow in the region of the cystic duct. No change took place in the shadow twelve hours after the tetiothalein sodium was given.

CASE 7.—A woman, aged 37, had had attacks of gallstone colic for seven years. She had no jaundice and had never been severely ill. Physical examination showed no changes of especial interest. Cholecystography was done. The roentgenogram before dye administration revealed a large dense sausage-shaped shadow in the region of the gallbladder and a ring-shaped shadow in the region of the cystic duct. There was no change in the size and density of the shadow in roentgenograms taken after dye administration, but there was a change to a dumb-bell shaped form. A roentgenogram twenty-four hours later showed further change in form.

Patients 6 and 7 were not operated on, but in view of the similarity of roentgenographic observations in them and the other patients a diagnosis in each case of cholelithiasis with cystic duct obstruction and subsequent deposition of calcium carbonate in the gallbladder and on the cystic duct stone was made.

Fig. 4 (case 1). — Roentgenographic appearance of specimen showing (a) large dense stone in gallbladder and (b) dense shadow on gallbladder side of cholesterol stone in cystic duct.

Fig. 5 (case 1).—Gallbladder and cystic duct incised showing (a) white stone in gallbladder and (b) gray cholesterol stone in duct with white deposit on its gallbladder side. Thick mucus containing white flecks filled the rest of the gallbladder.

COMMENT

It appears that the order of development of changes was as follows: First there was cholecystitis and cholesterol or cholesterol-pigment stone formation. The controversy as to the relationship between these two processes and as to which one precedes the other need not be discussed here. The cholecystitis was mild to moderate in grade, the mucosa showing the most marked changes, and the stones were multiple in at least five of the seven cases. A stone then passed into the cystic duct, lodging at various levels from the orifice to the common duct end. The obstruction was of high grade and in some cases the passage of bile into and of secretion out of the gallbladder appeared to have been completely blocked. Thus, in six cases tetiothalein sodium was administered and in no instance was there a shadow indicative of dye in the gallbladder region. The cholecystitis resulted in moderate thickening of the gallbladder wall and in serous exudation, but in no case was the gallbladder larger than normal and in most cases it was contracted. A moderate to a large amount of mucus was poured out. Calcium carbonate and a trace of calcium phosphate were then excreted by the wall of the gallbladder, forming a semisolid to soft white stone, incorporating other stones when they were present.

Hastings and Zachariasen of the University of Chicago demonstrated by x-ray spectrograms that the calcium carbonate present in three cases was in the crystal form of aragonite. The indications are that these calcium carbonate stones are formed only when bile is excluded from the gallbladder by the obstructing stone or when the amount entering it is greatly reduced. There is probably variation in the degree of obstruction in some cases with the variations in the amount of infection in the gallbladder and duct. The only direct references found to the subject were by Kaufmann,[2] who in discussing the pathologic condition of the gallbladder in cystic duct obstruction says that in some cases the gallbladder wall is degenerated and its cavity

2. Kaufmann, E.: Lehrbuch der pathologischen Anatomie, Berlin, W. de Gruyter & Co., 1922.

filled with a mortar-like mass of calcified thick secretion, and by Volkmann, who found the duct obstructed in one case.

No explanation has been found for the selective excretion of calcium carbonate over long periods of time in such cases, giving rise to these large white masses. It may be that it occurs only when the inflam-

Fig. 6 (case 2).—Appearance before administration of tetiothalein sodium. The dense shadow is due to calcium carbonate, and the negative shadows are due to incorporated cholesterol and bile pigment stones.

matory process and the obstruction are of certain degrees of severity and chronicity. Certain it is that in most cases of cholelithiasis with cystic duct obstruction and hydrops, calcium carbonate stones are not formed. In the cases here reported the inflammation appeared to be mild and chronic and there was no history pointing to the previous existence of a severe acute cholecystitis. Wilkie [3] reported that, when he produced cholecystitis in rabbits by bacterial injection and ligated the cystic duct, gallstones rich in calcium were formed but that, when the duct was not ligated, stones composed of cholesterol formed. Naunyn [4] asserted that the calcium carbonate of all gallstones is poured out in connection with the mucin formed by the epithelium of the gallbladder. This is supported by the fact that the only other calculi consisting of as high a percentage of calcium carbonate are found occasionally in the salivary ducts [5] and in the pancreas,[6] where there is also mucous secretion.

The question arises as to whether or not the calcium carbonate deposited in layers on cholesterol or mixed cholesterol-bile pigment stones is excreted by the gallbladder during periods of temporary obstruction of its outlet.

3. Wilkie, A. L.: The Bacteriology of Cholecystitis: A Clinical and Experimental Study, Brit. J. Surg. **15**: 450 (Jan.) 1928.
4. Naunyn, B.: Die Gallensteine, Jena, 1921.
5. Bessner, G.: Lehrbuch der physiologischen Chemie, 1874; quoted in Roberg: Sialolithiasis, Ann. Surg. **39**: 669, 1904.
6. Rosenthal, M.: Ein Beitrag zur Kenntnis der Lithiasis pancreatica, Arch. f. Verdauungskr. **20**: 619, 1914.

CALCIFICATION OF THE GALLBLADDER

In cases of chronic calculus obstruction of the cystic duct with extensive degeneration and fibrosis there may be calcification of the gallbladder wall and of the wall of the cystic duct about the impacted stone. In three autopsy specimens that have been studied the cystic duct was completely blocked and the epithelial lining and glands of the gallbladder were entirely destroyed. The wall of the gallbladder was converted into fibrous tissue and the calcareous deposits were irregularly distributed throughout it. The wall of the cystic duct and the surface of the stone were fused by a calcareous deposit where they were in contact. In the gallbladder shown in figure 7 a chemical analysis of the calcareous deposit showed that it consisted almost entirely of calcium phosphate, which amount is unusually high for calcified tissue, although this process has the appearance of ordinary calcification of degenerating tissue. In a fourth case of calcification of the wall of the gallbladder the cystic duct was not obstructed by a stone but the gallbladder lumen was filled by a large stone and the cystic duct was obliterated by fibrous tissue at its orifice so that no bile entered the gallbladder. A review of articles on calcification of the gallbladder by Robb,[7] Talbot,[8] and Fowler [9] brings out the fact that the cystic duct was obstructed either by stone or by scar tissue growing over its orifice in nearly all the reported cases, although no special attention was called to the relationship between the obstruction and the calcification. In none of our cases was there found a combination of a calcium carbonate stone in the lumen of the gallbladder and calcification of the gallbladder wall, but Robb has reported a case which from the illustration appeared to be such. Robb believes that in some cases hypercontraction is produced by the stones, leading to fibrosis and calcification of the walls.

Fig. 7.—Roentgenographic appearance of specimen; cholesterol-pigment stone obstructing cystic duct with calcification of (a) wall of gallbladder and (b) wall of cystic duct and surface of stone.

CONCLUSIONS

1. Large calcium carbonate stones may form in the gallbladder in cases of cholelithiasis and cholecystitis with chronic obstruction of the cystic duct by a stone, and it appears that duct obstruction is essential for their formation. The calcium is apparently excreted by the mucosa of the gallbladder.

7. Robb, J. J.: Observations on Calcification of the Gall Bladder with the Presentation of a Case, Brit. J. Surg. **18**: 114 (July) 1928.
8. Talbot, F.: Cholelithiasis: Notes on a Case with a Calcified Gall Bladder, Brit. J. Surg. **9**: 533 (April) 1921.
9. Fowler, W. F.: Calcareous Changes of the Gall Bladder Wall, Ann. Surg. **78**: 623 (Nov.) 1923.

2. Calcium may also be deposited on the stone in the duct, so that the diagnosis of its presence as well as that of the calcium carbonate stones in the gallbladder may be made from roentgenograms.

3. Calculous obstruction of the cystic duct followed by extensive degeneration and fibrosis of the gallbladder may result in marked calcification both of its wall and of that of the cystic duct at the point of impaction.

"LIVER DEATHS" IN SURGERY OF THE GALLBLADDER *

CHARLES GORDON HEYD, M.D.
Professor of Surgery, New York Post-Graduate Medical School and Hospital
NEW YORK

From time to time there have appeared in the medical press a number of papers analyzing the causes of death following operations on the gallbladder and ducts. In a recent contribution by E. M. Stanton, 500 fatal cases were analyzed in a combined series of approximately 10,000 gallbladder operations. Even on casual reading one is impressed with the number of ascribed causes of death in this series wherein over thirty-eight individual causes were designated as the lethal factor. The causes of death given in the order of their frequency were peritonitis, pneumonia, embolism, cardiac failure, spontaneous perforation, sepsis and renal failure. It is rather surprising that so-called shock and hemorrhage constituted 10 per cent of the fatal cases.

In analyzing our mortalities at the New York Post-Graduate Hospital we were impressed with a small group of fatal cases in which the cause of death could in no way be placed under such obvious types of mortality. There was about this group of cases an unexplained chemical mechanism as the outstanding feature in the production of death, and which was directly sequential to operative intervention.

We were able to distinguish with variations three distinctive types of death following gallbladder surgery and for want of a better term we have designated them as "liver deaths" and apparently due to a change in the physiologic status of the liver-gallbladder unit.

Type 1 is best depicted by a history of a typical case. A woman, aged 37, entered the Post-Graduate Hospital complaining of gas after eating and occasional pain in the right upper quadrant. There had been one attack of pain requiring a hypodermic of morphine. On examination the blood count was normal, the Wassermann test was negative and a phenolsulphonphthalein test for kidney function was normal. The patient was operated on at 9 o'clock in the morning. A simple cholecystectomy was performed, the common duct was not involved, and nothing noteworthy was found in the pancreas or in the remainder of the abdomen. The liver, however, showed a slight enlargement. The edges were crenated, the consistency was leathery. From the area of the gallbladder region was a white, rosette-like tissue, extending well over the dome and inferior surfaces of the right lobe of the liver. The patient had a simple ether anesthesia. The immediate postoperative reaction was normal. However, the patient did not completely come out from the anesthetic and was not awake by 3 o'clock in the afternoon. At the end of twelve hours the patient was decidedly lethargic or semicomatose and there was a gradual ascent in temperature, successively through 102, 103, 104, 105 and 106 F. The pulse rate and respiration paralleled the temperature rise. The chemical examination of the blood showed a normal icteric index and a gradual ascending scale of urea nitrogen. Clinical examination of the lungs gave no evidence of pneumonia. The patient died at the end of thirty-six hours.

We know that there is a close association in temperature regulation between the heat center of the brain and the heat production in the liver, as one third of the heat production of the body is due to liver activity. According to Crile, when the temperature of the liver is reduced 1 degree the chemical activity of the organ is reduced 10 per cent and it is possible when the abdomen is opened for the temperature of the liver to fall from 1.5 to 3 degrees even if the viscus is not directly exposed. Furthermore, when as the result of hepatic exhaustion incident to disease or surgical intervention, the chemical activity of the liver is reduced to 10 per cent of its normal capacity, death will occur. The anatomic result of cholecystectomy is the removal from the liver of an infected gallbladder, leaving a gallbladder fossa of varying degree of surface area capable of protein transudation and absorption together with a sudden change in the hydrostatics of bile flow.

Deaver, Pfeiffer, Sudler and Braithwaite have contributed noteworthy papers on the lymphatic and vascular association of liver, gallbladder and pancreas, and to a lesser extent of the viscera of the lower abdomen. It is not without significance that there is no anatomic block in the lymphatics between liver and gallbladder, the lymphatic channels passing uninterruptedly from gallbladder to liver and from liver to gallbladder. It is also noteworthy that lymphatic drainage from the area of the cystic duct and Calot's triangle is along the common duct to the under surface of the pancreas. The clinical association of pancreatitis and gallbladder disease is not without its effect on the reparative power of the patient. In addition to the functions usually ascribed to the liver, there is the ability of the bile acids to combine with the alkaline metals. The gastric chyme which leaves the stomach has an acidity of p_H 3 and is neutralized by an alkaline bile to give a duodenal mixture of a p_H of approximately 11. In alkalosis there are some changes in these differentials, but up to date we have found no constant factor of variation.

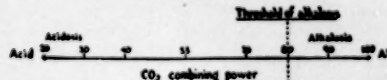
Clinical and laboratory studies indicate that both acidosis and alkalinity are associated with marked liver impairment and ketogenesis, and later with secondary kidney failure. In the type of mortality listed under type 1 there was no evidence in the preoperative study to indicate any renal impairment, either actually or potentially. In the past five years we have had fourteen gallbladder cases with a carbon dioxide combining power of over 80 volume per cent and of this group six patients died, with a clinical picture of stupor, hyperpyrexia and rapid death. In the fatal cases no alkali had been administered preoperatively and all exhibited a condition of pronounced alkalosis, as shown in the accompanying chart.

Type 2, a form of liver death much more infrequent than type 1, has occurred in patients who have had a previous cholecystectomy and rarely a drainage of the common duct. The patient is jaundiced, and the secondary operation consists of a choledochotomy, with T tube drainage. For the first few days after operation the postoperative course is normal and satisfactory.

* Read before the Section on Surgery, General and Abdominal, at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 11, 1931.

Then there is a distinct change in the character of the drainage. The biliary discharge becomes less and less in amount and more watery in consistency. In spite of the constantly diminishing jaundice, as shown by the decreasing icteric index, the patient becomes delirious; there is marked cerebral excitation, subsultus tendinum and carphology occur and finally stupor and coma. There is no clinical evidence of intra-abdominal hemorrhage or infection, yet in spite of a diminishing jaundice, coma develops, which in all of its clinical manifestations is similar to that which occurs in a terminal cholemia. By reason of the marked cerebrospinal irritation, spinal puncture has been made and practically normal fluid obtained with a slight globulin reaction and cell count of 9 or 10 cells per cubic millimeter. What has been the effect of the more or less sudden removal of the common duct obstruction? Have we induced a secondary acute reactive hyperemia in an already compromised liver? Do the liver cells function for a short time postoperatively and then fail?

Type 3 occurs much less frequently than either type 1 or type 2 and apparently is more amenable to treatment. These patients have diseases of the common duct and pancreatitis, do not have jaundice, and for the first twenty-four to thirty-six hours after a choledochotomy with T tube drainage have an apparently normal postoperative course. Then the pulse rate becomes markedly accelerated. The patient becomes markedly prostrated, with a fall in blood pressure and



An increase in the carbon dioxide combining power toward 80 indicates an alkalosis; the reverse, an acidosis.

a cessation of urinary secretion, and exhibits cold, clammy, moist extremities. The abdomen is without any clinical evidence of infection, hemorrhage or any unusual postoperative abdominal condition. A negative gastric lavage demonstrates an empty stomach and no gastric dilatation. One is impressed that while the clinical condition herein presented is very similar to shock it occurs from twenty-four to thirty-six hours after the operation and seems to be a complete vasomotor collapse from an overwhelming intoxication, probably of pancreatic origin. Transfusion and repeated infusions of physiologic solution of sodium chloride with 10 per cent dextrose are usually sufficient to save the patient.

From a practical point of view, the acid-base balance of blood plasma should be accurately determined preoperatively in all cases of gallbladder disease.

In the postoperative treatment of gallbladder cases, chief consideration should be given to the following:

1. A continuous and persistent effort should be made to combat the dehydration. This is best accomplished by using known quantities of fluid, through all channels —water with 10 per cent dextrose in the form of the rectal drip, physiologic solution of sodium chloride with 5 per cent dextrose by hypodermoclysis and physiologic solution of sodium chloride with 5 or 10 per cent dextrose solution intravenously. If the carbon dioxide combining power tends to the left, indicating a condition of acidosis, the dextrose is particularly beneficial because in the oxidation of dextrose there is a destruction of the ketogenic bodies. If the carbon dioxide combining power moves to the right, indicating an alkalosis, the administration of dextrose is primarily to prevent dehydration and in an important but secondary rôle to prevent protein destruction.

2. When vomiting is a conspicuous feature, with or without tetany, gastric rest should be maintained by an indwelling intranasal (Levine) tube.

3. If symptoms of tetany appear, 5 cc. of a 10 per cent solution of calcium chloride is given intravenously and repeated in eight hours if necessary.

4. Sodium bicarbonate should not be used in any form. As sodium bicarbonate is frequently employed for gastric lavage, it is particularly important to bear this point in mind.

5. It is essential to make repeated chemical determinations of the blood to control or indicate further therapy.

116 East Fifty-Third Street.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. PHEMISTER, REWBRIDGE AND RUDISILL, AND DR. HEYD

DR. DAMON B. PFEIFFER, Philadelphia: Dr. Phemister's contribution is another example of the fact that the cholecystogram is not an infallible indicator of the presence or absence of a surgical lesion of the gallbladder. This is not said in detraction of this valuable test, but the knowledge that false positives and negatives exist should sharpen the attention of the radiographer and the clinician. Dr. Heyd has drawn attention to a group of fatalities not readily explainable under the common causes of death. In some it seems probable that the outcome is due to some derangement, not thoroughly understood, of certain essential hepatic functions. It is well to appreciate the dangers that lurk in operations on individuals with a damaged liver. I should deprecate, however, the too facile adoption of such terms as "liver death" or "liver shock" to cover such deaths as appear mysterious and unexplainable. I suspect that some are not due to disordered hepatic chemistry but to fulminating infection of a sort not readily demonstrable. It is realized, as Dr. Heyd has said, that some of these deaths are due to disturbance of the acid-alkali balance of the blood, a condition that is usually preventable, and often remediable if recognized promptly and treated appropriately. I urge the more general adoption of his advice to employ the laboratory aids in detecting and in treating intelligently such chemical abnormalities. Alkalosis is especially liable to occur in connection with upper abdominal surgery. In all cases of so-called gastric dilatation or prolonged vomiting this condition occurs to a greater or less degree. The stomach tube, abundant fluids, sodium chloride, and dextrose are the specifics. In this type of surgery I am constantly exhorting interns to keep the stomach empty and the circulation full. There are exceptions to all rules. I have a patient, operated on for a gallbladder condition, a large man, who reacted badly to anesthesia and vomited profusely for three days. He had a high fever and low urinary excretion. Clinically I should have thought that he would exhibit alkalosis. To the contrary, the laboratory showed that he had an acidosis, which was explainable by the fact that he had renal insufficiency. The retention of abnormal acids more than counterbalanced the loss of acid in the stomach contents, to which the alkalosis is usually due. The warning against the use of sodium bicarbonate as a routine measure for gastric lavage or rectal instillation is important. I am glad the routine sodium bicarbonate rectal instillation has gone into the discard. Acetone in the urine does not mean acidosis. It may be present in alkalosis, in which case alkali treatment would greatly increase the danger. To a certain extent it is no longer necessary to postulate unknown chemical disturbances to explain clinical disorders. A more general use of recent contributions to blood chemistry is of great importance to the surgeon.

DR. I. S. RAVDIN, Philadelphia: Dr. Phemister and his associates have presented an extremely interesting pathologic

picture of the calcium carbonate stone. One might speculate as to why hydrops did not occur more frequently in these cases. In my studies on calcium absorption from the gallbladder I have found that in the damaged gallbladder the bicarbonate concentration increases above blood level and at this time calcium is precipitated from the solution. The precipitation first occurs under the mucosa of the gallbladder, and as this increases the mucosa disappears and a calcium carbonate plaque occurs on the surface of the mucosa with mucosal degeneration. Undoubtedly certain of the deaths reported by Dr. Heyd are due to ligation of the hepatic artery which may be in an anomalous position. If this ligation is done accidentally at operation, death will occur in from twenty-four to forty-eight hours from hypoglycemia and an increase in nitrogen content in the blood, regardless of the type of therapy that is instituted. I have felt that anesthesia is an important factor in these cases. For some time I have preferred spinal anesthesia. Ether can at times, especially if previous liver injury exists, cause marked liver necrosis with an associated hyperpyrexia and nitrogen retention. The existence of alkalosis in the cases described by Dr. Heyd may have been due to persistent vomiting, as Dr. Pfeiffer said. I have felt that slow decompression of an overdistended bile duct is an important factor in these cases. It is well known that portal obstruction occurs with bile duct obstruction, and in perfusion experiments of the hepatic artery and portal vein, obstruction of the bile duct results in a steady retardation of blood flow into the liver. A sudden release of this pressure in the bile ducts causes an acute reactive hyperemia of the liver, and there is no doubt that in certain of these cases, death similar to the death that occurs after an acute decompression of an overdistended bladder may occur. I have been using a simple method based on the work of Gamble for correcting dehydration in my cases. I feel that it is more important to correct dehydration than to correct blood reaction. If the dehydration is associated with salt loss, physiologic solution of sodium chloride is used; if it is associated with fluid restriction, tap water is given by rectum. If ketosis exists, dextrose is given either with or without physiologic solution of sodium chloride intravenously.

DR. P. B. SALATICH, New Orleans: I was greatly interested to hear Dr. Heyd talk about some of these deaths that he couldn't account for. I am going to try to explain some of those unaccountable deaths. I shall take it for granted that the patient has been thoroughly studied before operation and that the proper technic is carried out in operating. I mean by proper technic that the cystic duct is carefully dissected and not mass forceps put on, catching lymph nodes (for very often there is a chain of lymph nodes right at the cystic duct) and that the gallbladder is removed, as is usually done, and so on. First is the interference with the liver function. That is a big subject with which all of us are concerned. For years I have been using epinephrine, with excellent results, and I know that epinephrine helps liver function. If I have a bad case I give epinephrine frequently in repeated doses, and if one gives solution of epinephrine to a normal patient, he gets a pretty good reaction from ten drops. In a patient whose liver function is interfered with, if one gives 10 minims of solution of epinephrine one can repeat that every three hours and that patient has very little reaction. After twelve, twenty-four hours, or more, the liver function, I believe, is restored, my patient begins to get quite a reaction from the epinephrine. Then I either stop or diminish the dose, depending on how bad the case is. I think it is wrong to wait until one can see the bulging of the stomach before introducing a tube. Very often one will find that twelve hours afterward the patient will have a good deal of ugly material in the stomach, and the stomach does not appear distended. Some of the patients that die in an unexplainable manner run along for twelve or twenty-four hours doing well, and then suddenly they become distended; they get depressed and have cold, clammy sweats and kidney interference and very often there is a history of alcoholism. There are three important danger signs: high temperature, acetone in the urine, and dilatation of the stomach. The patient may have either one of them alone and recover, but when he has all three together, generally the mortality is high.

DR. MOSES BEHREND, Philadelphia: I believe that we have all encountered these sudden deaths after cholecystectomy, and, as Dr. Heyd has stated, the causes vary. They have been called liver deaths, but there are many causes about which nothing is known. Certainly chemistry plays an important part in the causes of death of these individuals. I have operated on patients, performed a cholecystectomy, and within twenty-four hours the temperature would rise to 106 and even 108 F., and the patient would die within twenty-four hours. These deaths are unexplainable. I believe there will be less of these liver deaths on account of the use of spinal anesthesia. I believe that in former years, prior to the universal use of spinal anesthesia, many deaths were due to rough handling of the site of operation. Spinal anesthesia has eliminated that altogether. One can make a dissection, such as has been spoken of here, in a very anatomic manner. There is another cause of death, and that is operating on acutely inflamed gallbladders. One should never operate on an empyema of the gallbladder in the acute stage. The great danger in waiting is supposed to be rupture of the gallbladder. I have seen only one rupture of the gallbladder in thirty years. I am sure that this need not be considered as an argument to operate on an empyema of the gallbladder immediately; an empyema of the gallbladder should be operated on a week or ten days after the inception of the attack. Ligation of the hepatic artery has been mentioned. I have done a lot of experimental work on the ligation of hepatic arteries, and I am sure it is one of the causes of death in these cases. Last year, I operated on a physician of this state and found a thrombosis of the hepatic artery. One half of the liver was pale and anemic; the other half was of normal color. In addition, he had an empyema of the gallbladder, which contained many stones; the gallbladder was removed. At the time of operation I told his accompanying physician that this case was a very serious one on account of the anemia of half of the liver. This is the first time I have seen a case of this sort.

DR. CHARLES GORDON HEYD, New York: I think the discussion has brought out that all have had the experience of standing at the bed of a patient on whom one has operated that morning. One asks oneself: "What is the mechanism that is killing that patient?" A few hours later the patient is dead. The death certificate is made out: terminal pneumonia, heart failure, or uremia, three insecure diagnoses—terminal events. Some chemical change has taken place; whether it has been the unfortunate misadventure of the time of operation or something else, the result has been sequential to the operative intervention.

DR. DALLAS B. PHEMISTER, Chicago: In reply to Dr. Raydin as to the source of the calcium in these two types of lesions, there can be no question about its coming from the blood stream in the case of calcification of the wall of the gallbladder. No bile is entering the gallbladder, and calcium phosphate and calcium carbonate are deposited in its degenerating wall as in the calcification of other tissues. There is more question about the origin of the calcium carbonate which forms the gallstones. However, I believe that it is secreted by the mucosa of the gallbladder in the presence of obstruction of the duct. One of the stones weighed 18.5 Gm. and it is difficult to conceive of that amount of calcium carbonate coming from bile working by a large stone obstructing the cystic duct.

Etiology of Endometriosis.—In 1908 Cullen examined a number of specimens of diffuse endometrioma of the uterus, or diffuse adenomyoma as it was then called, and found as a result of his investigations that in places there was direct continuity between the endometrium proper and that contained within the tumor, and frequently an actual communication between the uterine cavity and several of the cystic spaces in the growth. This became known as the diverticular theory, and may be regarded as the simplest form of endometriosis. In certain other uterine endometriomata no such continuity can be demonstrated, and in these it must be assumed that the misplaced endometrium has reached its new situation by metastasis through the lymph vessels or venous channels of the uterine wall. Similar tumors not infrequently follow tuberculosis of the uterus or tubes, so it is possible that an inflammatory process may be a factor of some importance.—Dougal, D. D.: Remarks on Endometriosis and Endometriomata, *Brit. M. J.*, Nov. 21, 1931, page 929.

NEUROLOGIC SYNDROMES ASSOCIATED WITH HYPOGLYCEMIA *

ARCHIE D. CARR, M.D.
ST. LOUIS

Hypoglycemia as the cause of a variety of neurologic pictures has been most forcefully brought to attention during the past year by the coincidence of several similar cases which appeared in Barnes Hospital. One of these, which was referred to us with a previous diagnosis of epilepsy, was found to show a classic picture of hypoglycemia caused by an adenoma of the pancreas.[1] It was possible to demonstrate and remove the adenoma, with the disappearance of hypoglycemia and the clinical cure of the patient. A patient of Womack, Gnagi and Graham,[2] in whom an adenoma of the pancreas was demonstrated, had had periods of confusion and convulsive movements for over a year, had been placed on phenobarbital and considered as a brain tumor suspect. Another case,[3] diagnosed as syphilis of the nervous system, terminated fatally in convulsions. At autopsy a small adenoma of the pancreas was found.

ETIOLOGY AND INCIDENCE OF HYPOGLYCEMIA

Evidence accumulated during the past few years has demonstrated that hypoglycemia is by no means a rare condition. In its study, various workers have rather arbitrarily placed the fasting blood sugar level at figures ranging from 70 to 90 mg. per hundred cubic centimeters of blood, the most generally accepted level being 70 mg. or lower.

Since the discovery of insulin, values for blood sugar below normal levels have been described in a number of pathologic conditions. Seale Harris,[4] in 1924, first hypothecated a "hyperinsulinism" which should produce a definite picture of hypoglycemia and its concomitant symptoms. At that time he reported three cases with fasting blood sugar levels from 47 to 67 mg. per hundred cubic centimeters which showed weakness, ravenous hunger and nervousness. Harris advanced the idea that hyperactivity of the islands of Langerhans causes the sensation of hunger and a greatly increased consumption of carbohydrates.

Experimentally, many drugs having a toxic action on the liver, such as chloroform, phosphorus and hydrazine, will produce a hypoglycemia apparently secondary to the decreased glycogen store in the liver. Removal of parts or all of the liver causes a marked or fatal hypoglycemia.

Porges,[5] working with cats, states that the removal of the suprarenals is followed by a hypoglycemia reaction.

Jonas,[6] in his survey of the literature, pointed out that hypoglycemia is found associated with so many conditions that it may be ascribed as a causative factor in the production of weakness and easy fatigability.

Holman[7] cites three cases, one in detail, which, twenty-four hours following subtotal thyroidectomy, showed low blood sugars with symptoms of semistupor, extreme restlessness and marked weakness. He calls attention to the fact that the immediate effect of the active thyroid substance is to produce a tremendous increase in general body metabolism, necessitating a utilization of all the available carbohydrates, including the glycogen reserve in the liver and in the muscle tissues. Eventually, if sufficient active substance has been taken up by the circulation, the consumption of all available carbohydrate takes place and hypoglycemia supervenes.

Schwarz,[8] in 1926, reported a case in which a patient in late pregnancy suffered from moderate hyperthyroidism. This patient, following a sugar tolerance test, showed a series of low blood sugars with complaints of weakness, nervousness and periods of anxiety. He suggested that these lowered blood sugars could be accounted for by a combination of two factors: the storage of carbohydrates by the fetus during late pregnancy and the depletion of glycogen stores consequent on the hyperthyroidism.

During the past few years, several authors have presented cases of hyperinsulinism due to disease of the pancreas. In 1926, Warren[9] was able to collect fifteen cases of benign tumors of the pancreas and report five of his own. In his series he studied only the pathology, with no correlation of clinical and pathologic data. Margaret Smith,[3] in searching for the cause of death in a patient who had been known to have syphilis, found an adenoma of the pancreas. Blood sugar as low as 58 mg. per hundred cubic centimeters had been recorded in this case.

Wilder and his co-workers[10] stimulated interest in hypoglycemia and hyperinsulinism by their classic study of a case of carcinoma of the pancreas. It was demonstrated that the hypoglycemia was definitely associated with an overproduction of insulin and its constant liberation into the blood stream.

Thalhimer and Murphy[11] report a case of adenoma of the pancreas, demonstrated at autopsy, which occurred in a patient who, for two and a half years, had suffered from attacks of stupor which had been complicated by epileptiform seizures during the year before death. At no time during the observation of this patient had the blood sugar been over 60 mg.

McClenahan and Norris[12] likewise reported a case of adenoma of the pancreas demonstrated at autopsy, in which hypoglycemia was present. Howland and his co-workers[13] reported the first cure by removal of a tumor of the pancreas in a patient with hypoglycemia.

Allan[14] and others have reported cases of hypoglycemia not necessarily due to focal disease of the pancreas, yet presenting as characteristic a picture. Hartmann,[15] in 1929, added a case in a man, aged 43, with blood sugars as low as 32 mg., who died with symptoms suggesting hypoglycemia.

Waters[16] reported three cases of paroxysmal tachycardia associated with hypoglycemia and repeats the belief that prolonged high carbohydrate diet stimulates

* From the Department of Neurology of Washington University and the Barnes Hospital.

* Read before the Section on Nervous and Mental Diseases at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 11, 1931.

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16. Waters, W. C., Jr.: South. M. J. **24**: 249 (March) 1931.

excessive insulin formation with a resulting spontaneous hypoglycemia.

Suprarenalectomy may be accompanied by hypoglycemia and, according to Britton and Silvette,[17] may be controlled by the use of extracts of suprarenal cortex, prepared according to the method of Swingle and Pfiffner. This cortico-suprarenal hormone, however, has no effect in relieving the hypoglycemia and convulsive reactions following the administration of insulin, varying in this respect from epinephrine.

SYMPTOMATOLOGY

Nervous symptoms form a predominant part of the clinical picture of hypoglycemia. They are varied and numerous, although not all of them are present in any one case. They seem to depend on the hypoglycemia itself and are not materially modified whether the lowered blood sugar is caused by administration of insulin, by liver damage or by pancreatic tumor. The intensity of symptoms, moreover, seems to bear a more or less definite relationship to the degree of hypoglycemia. Moderate lowering of blood sugar values is accompanied by ravenous hunger, sweating, restlessness, anxiety, and weakness which has been so striking as to suggest to some observers that cases of supposedly organic weakness may have a similar origin. McCrudden and Sargent[18] believe that the hypoglycemia (64 mg. per hundred cubic centimeters) in their case of progressive muscular atrophy was the cause of extreme weakness, for when they increased carbohydrates sufficiently to raise the blood sugar level they brought about an increase in strength and weight.

Nervous Symptoms in Spontaneous Hypoglycemia

Author	Cause of Hypoglycemia	Nervous Symptoms
Holman	Thyrotoxicosis	Stupor, restlessness, weakness
Schwarz	Hyperthyroidism; late pregnancy	Nervousness, anxiety, weakness
Smith	Adenoma of pancreas	Stupor; convulsions
Wilder et al.	Carcinoma of pancreas	Restlessness; anxiety; stupor; convulsions
Thalheimer and Murphy	Adenoma of pancreas	Periods of stupor, convulsions
Howland et al.	Adenoma of pancreas	Hemiparesis with slurring speech, stupor, convulsions
Hartmann	Unknown	Weakness, diplopia, confusion, stupor, convulsions
Womack et al.	Adenoma of pancreas	Confusion, stupor, convulsions
Carr et al.	Adenoma of pancreas	Diplopia; confusion, stupor, automatic behavior

With more advanced hypoglycemia, patients become more stuporous, usually completely amnesic, not infrequently comatose. There may be twitching or actual convulsions, which have been mistaken for those of idiopathic epilepsy. Deep reflexes are diminished or abolished. Hemiparesis disappearing with restoration of normal blood sugar level was reported by Howland. Death may occur during the attack, but many cases have shown a surprising and somewhat mysterious tendency toward recovery after the attack has fully developed.

The picture of hypoglycemia resulting from overdosage of insulin is too well known to require any elaboration. It is of some interest, however, to detail the nervous symptoms that have been reported in connection with spontaneous hypoglycemia from different origins. These may be seen in the accompanying table.

Several of these cases are of such interest as to merit further comment. Womack, Gnagi and Graham's patient was a man, aged 44, who had had periods of confusion for over one year, a tentative diagnosis of cerebral tumor had been made, and the patient had been placed on phenobarbital. The attacks consisted of periods of confusion, talking at random, and convulsive movements.

Hartmann's patient with a definite hypoglycemia died of status epilepticus in an epileptic colony.

In Howland's patient, following several of the attacks of stupor the left arm and left leg were paretic, and, while at first this lasted only a few hours, in later attacks it remained for several days and was associated with a thick slurring speech.

In our patient it was possible to follow the progress of symptoms on several occasions over periods of from six to eight hours. With fasting blood sugars of from 72 to 86 mg. there were no symptoms. When the blood sugar fell to between 60 and 65 mg., there was restlessness, apprehension, and sweating with lethargy. Below the 60 mg. level the patient was unresponsive but moved with stimulation. With the level between 36 and 48 mg. the patient could not be aroused and had involuntary muscle movements of a convulsive character.

The outstanding feature of the history consisted of periods of sudden onset in which activity was continued, but with complete amnesia. On one occasion, about a year before he was first seen, the patient was dressing for mess, heard the bugle, but remembered nothing more until he found himself being examined by the adjutant. He had dressed clumsily, had appeared in the mess hall and had awkwardly begun to eat, when it was suspected that something was wrong. At another time, while with a friend, he had driven through a fairly busy section of a large city, had at least one minor accident, paid for the damage, and later had no recollection of the drive. During each of these episodes, behavior was entirely automatic, permitting him to dress himself and to drive an automobile. Following each of these episodes, he became stuporous and remained so for some hours. On the first occasion he remained stuporous for thirty-six hours before some compensatory and life-saving mechanism caused him to become sufficiently alert to take food, which promptly cured the attack.

COMMENT

The mechanism of the spontaneous recovery from fully developed attacks of hypoglycemia is by no means clear. Cannon, McIver and Bliss,[19] in experiments on cats, demonstrated a mechanism or series of mechanisms having the function of maintaining the physiologic percentage of blood sugar when there is danger of deficiency. They state that, if the blood sugar falls below a critical point in consequence of a deficiency, the splanchnic neurons of the sympathetic system are set in action as indicated by increased suprarenal secretion. Both the nerve impulses and the increased secretion of epinephrine have the effect of liberating sugar from the liver into the circulation, thus tending to restore the equilibrium.

In Wilder's and Howland's cases, as well as in ours, an increase in blood sugar was found following the administration of epinephrine; so at least in these cases there was an available supply of glycogen in the liver, which could be mobilized by such a mechanism. It

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seems possible that in our patient this mechanism might have been responsible for spontaneous recovery after fairly long periods of stupor.

In this discussion it is not intended to imply that idiopathic epilepsy or other common neurologic conditions have reduced blood sugar or that hypoglycemia is a frequent cause of amnesia or hemiparesis. It is apparent, however, that mistakes may easily occur and that the early recognition of this condition is of the utmost importance. The symptoms which have been detailed are so distinctive that they can hardly be missed if the condition of hypoglycemia is considered at all. Most important in the diagnosis, therefore, is to have the condition in mind. To confirm or reject the suspicion of hypoglycemia, it is only necessary to determine the blood sugar level, which today is so simply performed that it should not be omitted in any doubtful case.

SUMMARY

No matter what the cause, hypoglycemia may be manifested by stupor, amnesia, muscular twitching or convulsions and a number of less striking symptoms, such as restlessness, weakness, anxiety and fatigability.

Diagnosis of various functional and organic nervous diseases may be made if the condition of hypoglycemia is not considered.

The diagnosis of hypoglycemia depends on a careful history of preceding symptoms, the recognition of coexisting diseases and, above all, the determination of the blood sugar level.

3720 Washington Boulevard.

ABSTRACT OF DISCUSSION

DR. EUGENE F. TRAUT, Chicago: Dresel produced hypoglycemia by stimulating the vagus and caused hyperglycemia by stimulating the splanchnics. Some hold that the hypoglycemic symptoms are due to overaction of the suprarenals, an effort of the organism to reestablish its blood sugar equilibrium. The pallor, rise in blood pressure, and dilated pupils substantiate this. The usual immediate sequence of an insulin reaction is a rise in the blood sugar. The symptoms consequent on lowering of blood sugar depend on whose blood sugar one lowers. I have intentionally produced lowering in patients in certain conditions. I have lowered the blood sugar to 46 mg. per hundred cubic centimeters without producing any symptoms at all. Children stand a low blood sugar much better than do adults. A school teacher, aged 36, had taken large doses of insulin with varying diets over a long period. She experienced frequent attacks of headache, dizziness and diplopia before her meals. She had showed slight edema of the disks. She was referred to a neurologic surgeon, and under exact control of diet and reduction of insulin the signs and symptoms disappeared. A child, aged 4 years, entered the hospital in a deep coma from acidosis. Large doses of insulin were employed. Acetone bodies disappeared from the urine. The coma continued, but her body became spastic. There was opisthotonos. She had strabismus, dilated pupils and positive Babinski signs. The diagnosis of tuberculous meningitis was considered, as the spinal fluid sugar level was normal. There was, however, no pleocytosis. Reduction of the insulin brought her out of the coma. Her right hand and arm were paretic for many weeks. Apraxia of the right hand persists. A man, aged 64, had had both legs removed at the thigh for diabetic gangrene, thus reducing the body volume considerably. On discharge from the hospital he was given a diet. He was not seen until two years later and within those two years, retaining that diet and dosage of insulin, he had changed personality. He was irritable and, at times, violent. Morphine failed to control him. Withdrawal of the insulin abolished the symptoms. He remained sugar-free. Dr. Carr's diagnosis, followed by the successful removal of the causative pancreatic neoplasm, should serve to emphasize the necessity of more frequently considering the possibilities of hypoglycemia in patients showing suggestive symptoms.

DR. FRANK N. ALLAN, Rochester, Minn.: The symptoms attributed to hypoglycemia do not always correspond to the level of the blood sugar. In diabetic patients treated with insulin the symptoms sometimes appear when the blood sugar is not subnormal; in fact, they may occur when the blood sugar is above normal. I have seen distinct symptoms of hypoglycemia with the blood sugar above 0.3 Gm. per hundred cubic centimeters. On the other hand, a subnormal level of the blood sugar may exist without the appearance of any symptoms. The blood sugar may be as low as 0.04 Gm. per hundred cubic centimeters without any symptoms. There is need for investigation to determine the exact cause of the symptoms which are attributed to hypoglycemia. In the diagnosis of hypoglycemia it must be remembered that, if a test of the blood sugar is made at a time when the symptoms are not present, the condition may be overlooked. At the onset of hyperinsulinism, the blood sugar may be unstable; it may be normal, or even much above normal after food is taken. Even the fasting blood sugar test made in the ordinary way may be practically normal. In some cases it may be necessary to have the patient miss his meals and undergo strenuous exercise in order to induce the appearance of the symptoms and make recognition of hypoglycemia possible. After our experience with the case studied at the Mayo Clinic four years ago, in which a tumor of the islands of the pancreas was found, it was thought that early recognition of similar cases and early operation might lead to cure of the condition. This hope was realized when Howland, Campbell, Maltby and Robinson at Toronto reported their case two years ago. Since that time three cases of hypoglycemia, including the one described by Dr. Carr, have been cured by removal of a tumor. The prospect of cure by surgical treatment is not always so satisfactory. To my knowledge, operations have now been performed on ten patients with hyperinsulinism. In five a tumor has been found; in four it has been removed successfully with cure. In five cases the pancreas has appeared normal. Resection of part of the pancreas has brought about some benefit, but there has not been complete cure.

THE RÔLE OF THE FEMALE SEX HORMONE *

ROBERT T. FRANK, M.D.
NEW YORK

To describe the rôle of the female sex hormone ten years ago would have been a simple matter, as this hormone alone would have had to be considered, the main attention then being focused on the corpus luteum.[1] Four years ago the situation became more complicated when Philip Smith,[2] and almost simultaneously Zondek and Aschheim,[3] showed that the prepituitary was necessary to activate the ovaries. A further complication was added when Hisaw [4] discovered an aqueous corpus luteum factor which affected the pubic ligaments of the gopher, and Corner [5] concen-

* From the Gynecological Service and Department of Laboratories, the Mount Sinai Hospital.

* Read before the Section on Obstetrics, Gynecology and Abdominal Surgery at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 11, 1931.

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trated "progestin," the special lipoid extract of the corpus luteum.

Today, therefore, when analyzing the processes of the sex physiology in the female, it is necessary for one to consider all these chemical messengers. The structures to be analyzed now include the follicle,[6] which excretes

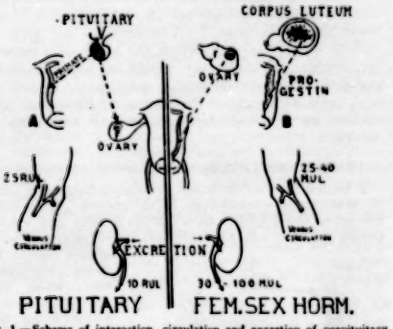

Fig. 1.—Schema of interaction, circulation and excretion of prepituitary and female sex hormones in the nonpregnant woman: To left: The prepituitary stimulates follicle (*F*) growth. In the castrate it can induce menstruation, according to Hartman (*A*). As much as 25 rat units per liter (R. U. L.) may be obtained from the venous blood; 10 rat units per liter from the urine. To right: The follicle (*F*) produces female sex hormone, which stimulates the endometrium, the rest of the tubular tract and the breasts. After ovulation the corpus luteum elaborates "progestin," causing the pregravid endometrial change (*B*). Before menstruation, from 25 to 40 mouse units per liter are recovered from the venous blood. From 30 to 100 mouse units per liter are excreted by the kidneys.

female sex hormone alone except in pregnancy, at which time prepituitary hormone also may be found in the follicular fluid, the corpus luteum, which elaborates not only female sex hormone but "progestin," the placenta from which female sex hormone,[1] prepituitary hormone,[7] and, according to Collip,[8] "emmenin," another prepituitary-like substance, have been obtained, as well as at least two fractions from the prepituitary gland.[9] With so many hormones acting either directly or indirectly on the sexual sphere, it is not surprising that a basic analysis of the many phenomena encountered proves difficult. Yet the great majority of clinicians are satisfied to arrive at diagnoses, based on single predominant symptoms such as amenorrhea, oligomenorrhea, menorrhagia or metrorrhagia, due, as I shall show, to a number of hormonal variations, without making any attempt to investigate the hormone contents of the body fluids and excretions, although methods for these hormonal determinations are now available. In other disciplines of medicine such neglect would be frowned on as, for example, the failure to determine the basal metabolic rate in thyroid disturbances, to obtain electrocardiograms in cardiac disease, or to study the blood sugar in diabetes.

The female organism, from the neonatal age to the menopause, and perhaps beyond this critical period, is under the influence of the prepituitary hormone and the female sex hormone. After puberty, it is affected at intervals by the progestational hormone. The mechanism by which the female sex hormone influences the female tubular tract and breasts is well known.[10]

To summarize these various endocrine influences, the anterior lobe hormone stimulates the ovary to produce follicles (fig. 1). The follicle in turn elaborates the female sex hormone, which reaches the tubular tract (tubes, uterus, vagina) by means of the blood stream.[11] The tubular tract, after sufficient blood concentration has been reached, then undergoes the early premenstrual changes. Following ovulation, the corpus luteum develops. This transitory gland continues to produce female sex hormone as well as a special hormone, whose presence in the circulation has not yet been demonstrated, enhancing the local uterine and breast changes necessary for the nidation and early nutrition of the fertilized ovum. Among these changes, sensitization of the uterine mucosa, requisite for successful embedding, is particularly important.[12] If the corpus luteum is removed at this early stage, the ovum fails to secure the necessary firm hold in the endometrium and abortion results.[13] The chorion epithelium, later developing into the placenta, an important gland of internal secretion, takes up the production of both female sex hormone and prepituitary hormone. Probably as a safety factor the circulation is flooded with these two internal secretory products to such a degree that an enormous amount is excreted through the kidneys [14] and bowel [15] throughout pregnancy (fig. 2).

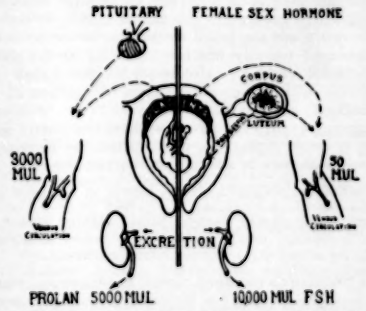

Fig. 2.—Similar schema of the pregnant female: To left: The prepituitary and placenta secrete prolan A and prolan B; 3,000 mouse units per liter can be recovered from the venous circulation, 5,000 mouse units per liter from the urine. To right: The corpus luteum and the placenta secrete female sex hormone (F. S. H.); 50 mouse units per liter can be recovered from the circulation, 10,000 mouse units per liter from the urine. "Progestin" is secreted by the corpus luteum at least during early pregnancy.

The clinical conditions to be covered in this paper have been limited arbitrarily to adolescents and mature women with functional disturbances. The discussion

6. Frank, R. T.: The Ovary and the Endocrinologist, J. A. M. A. **78**: 181 (Jan. 21) 1922. Allen, Edgar; and Doisy, E. A.: An Ovarian Hormone: Preliminary Report on its Localization, Extraction and Partial Purification, and Action in Test Animals, J. A. M. A. **81**: 819 (Sept. 8) 1923.

7. Philipp, E.: Hypophysenvorderlappen und Placenta, Zentralbl. f. Gynäk. **54**: 450 (Feb. 22) 1930.

8. Collip, J. B.: The Ovary Stimulating Hormone of the Placenta, Canad. M. A. J. **22**: 215 (Feb.) 1930; Placental Hormone, ibid. **23**: 631 (Nov.) 1930.

9. Zondek, Bernhard: Die Hormone des Ovariums und des Hypophysenvorderlappens: Untersuchungen zur Biologie und Klinik der weiblichen Genitalfunktion, Berlin, Julius Springer, 1931.

10. Frank, R. T.: The Female Sex Hormone, Springfield, Ill., Charles C. Thomas, 1929.

11. Loewe, S.: Nachweis brunsterzeugender Stoffe im weiblichen Blute, Klin. Wchnschr. **4**: 1407 (July 16) 1925. Frank, R. T.; Frank, M. L.; Gustavson, K. G., and Weverts, W. W.: Demonstration of the Female Sex Hormone in the Circulating Blood: I. Preliminary Report, J. A. M. A. **85**: 510 (Aug. 15) 1925.

12. Loeb, L.: The Function of the Corpus Luteum, the Experimental Production of the Maternal Placenta and the Mechanism of the Sexual Cycle in the Female Organism, M. Rec., New York **77**: 1083, 1910.

13. Fraenkel, L.: Die Funktion des Corpus Luteum, Arch. f. Gynäk. **68**: 438, 1903.

14. Aschheim, Selmar; and Zondek, Bernhard: Hypophysenvorderlappen und Ovarialhormon im Harn von Schwangeren, Klin. Wchnschr. **6**: 1322 (July 9) 1927.

15. Dohrn, M., and Faure, W.: Ueber die Ausscheidung des weiblichen Sexualhormons, Klin. Wchnschr. **7**: 943, 1928.

will be further limited to the group of cases in which we have studied the hormone content of the blood and excretions.

In order actually to confine the survey to these groups, it is first necessary to exclude organic causes such as tumors (especially fibroids) or infection of the genital tract. Next, we have found it essential to discover whether patients who show disturbances in their sexual sphere are free from other demonstrable endocrine disease, such as the well understood classic syndromes, for example, Froehlich's dystrophia adiposogenitalis, thyroid overactivity or underactivity (recognizable as exophthalmic or toxic goiters, and myxedema) for in these conditions the genital disturbances are usually secondary. I have purposely tried to eliminate these secondarily genital deviations, as far as possible, in order to simplify the already sufficiently complicated problems encountered.

Among the primary functional diseases of the female, hyperfunctional conditions have proved most difficult to analyze. They include bleeding, either excessive in amount or too frequent in occurrence, or a combination of the two, often accompanied by symmetrical enlargement of the uterus.

The hypofunctional conditions, on the other hand, can be classified under the general headings of amenorrhea (also oligomenorrhea) and sterility, which embrace the large majority of cases. Rarely, continuous bleeding is noted in patients whose hormonal examination has convinced us that the underlying disturbance is of hypofunctional nature. This apparently anomalous phenomenon emphasizes the fact that little or nothing is known about the actual mechanism of menstruation, which until recently has been ascribed to the abrupt withdrawal from the circulation of the female sex hormone, with consequent changes in nutrition of the stimulated endometrium, manifested by bleeding.[16] According to the most recent work of Hartman,[17] however, it would appear that menstruation can be brought on in the castrate by prepituitary hormone alone.

Whether the finding of a small number of red blood cells in the vaginal washings can be regarded as "menstruation" in the rhesus monkey (which species normally, as well as after preliminary female sex hormone injection, menstruates freely for several days) requires further confirmation.

In addition to the usual clinical examinations, which, in those cases which are worked up, include a careful history, anthropometric measurements, basal metabolism, differential blood count, and, when indicated, sugar tolerance, sellar roentgen and visual field examinations, certain hormone tests should be performed.

This does not signify that every patient with menorrhagia and metrorrhagia of short duration, or every obese patient with amenorrhea is put to the trouble and inconvenience of having to submit to all these tests. Were this the routine, both patient and physician would have just cause for complaint of the overemphasis on laboratory investigation. On the other hand, the patient who bled from her fourteenth to her twenty-eighth year, during which time she was thrice curetted, repeatedly subjected to radium application, and referred to internists, gynecologists and psychoanalysts without ever having a basal metabolism and blood hormone tests made, had just cause for complaint.

16. Allen, Edgar: The Menstrual Cycle of the Monkey, Macacus Rhesus: Contributions to Embryology, Carnegie Institution, Washington **98**:1, 1927.

17. Hartman, C. G.; Firor, W. M., and Grilling, E. M. K.: The Anterior Lobe and Menstruation, Am. J. Physiol. **95**:662 (Dec.) 1930.

The hormone tests which I advocate in properly selected instances include the evaluation of the female sex hormone blood level throughout a cycle, or, if no periodicity exists, over a period of from five to six weeks, with simultaneous determination of the hormone excretion through the urine. For the last six months we have extended our studies to the prepituitary hormone in the blood and urine, but are not as yet prepared to consider these data conclusive.[18] The technics are now sufficiently standardized to permit the study of a considerable number of cases each month in small laboratories not possessing special equipment.

A brief summary of the technic of these tests should suffice, as detailed descriptions are accessible elsewhere.[19]

FEMALE SEX HORMONE TEST OF THE BLOOD[19]

In testing for the female sex hormone, advantage is taken of its preferential solubility in lipoid solvents. The standard amount of blood used is 40 cc., which is dried with anhydrous sodium sulphate and fully extracted with ether. The ether soluble residue is injected into castrate mice, whose vaginal spread is examined according to the method described by Allen and Doisy.[20]

In the fully normal, fertile woman, one mouse unit can be demonstrated in 40 cc. of blood from seven days before the menses to the onset of menstruation (fig. 5 *A*).

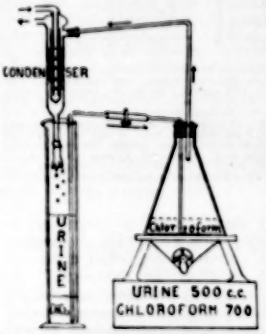

Fig. 3.—Apparatus for the automatic extraction of female sex hormone from the urine: The chloroform in a 2 liter flask on an electrical hot plate is distilled over and drips through the urine, collecting at the bottom of the cylinder. By siphonage it is returned to the flask, a 100 cc. turnover taking place every three minutes.

FEMALE SEX HORMONE TEST OF THE URINE

After Loewe[21] had shown that the female sex hormone appears also in the urine, our our attention was increasingly directed toward the amount excreted through the kidneys. We use a simple technic consisting of automatic continuous extraction by means of chloroform, which, if run for ten hours, completely extracts the hormone (fig. 3). By running a combined sample (500 cc.) of the total urine collected over three days, injecting the chloroform residue corresponding to 100, 75, 50 and 30 cc. of urine, the number of mouse units per liter (M. U. L.) from 10 to 30 are quickly determined. If larger amounts of hormone are demonstrated by these preliminary tests, injection of smaller doses of extract supplies the necessary data.

We have found that a normal woman excretes at least from 800 to 1,500 mouse units during an entire cycle. Two periods of maximum excretion correspond to the time of ovulation and from one to two days before menstruation (fig. 5 *A*).

18. Frank, R. T.; Goldberger, M. A., and Spielman, Frank: A Method for Demonstrating the Prepituitary Maturity Hormone in the Blood of Nonpregnant Women, Proc. Soc. Exper. Biol. & Med. **28**:999 (June) 1931.

19. Frank, R. T., and Goldberger, M. A.: The Female Sex Hormone: VIII. Simplification of Technic, J. A. M. A. **96**:374 (Feb. 4) 1928.

20. Allen, Edgar; Francis, B. F.; Robertson, L. L.; Colgate, C. E.; Johnston, C. G.; Doisy, E. A.; Komitz, W. B., and Gibson, H. V.: The Hormone of the Ovarian Follicle: Its Localization and Action in Test Animals, and Additional Points Bearing upon the Internal Secretion of the Ovary, Am. J. Anat. **34**:133 (Sept.) 1924.

21. Loewe, S., and Lange, F.: Der Gehalt des Frauenharnes an brunsterzeugenden Stoffen in Abhängigkeit vom ovariellen Zyklus: Ueber weibliche Sexualhormone: VII. Mitteilung, Klin. Wchnschr. **5**:1038 (June 4) 1926.

PREPITUITARY MATURITY FACTOR TEST OF THE BLOOD

Our technic for evaluating the prepituitary maturity factor in the blood is based on the extraction of the residual blood and sodium sulphate mixture previously utilized for study of the female sex hormone. This residual powder, after having been freed of its female sex hormone content, is extracted with 60 per cent alcohol, at which dilution the prepituitary hormone is fully soluble but only a minimal quantity of sodium sulphate is dissolved. The alcoholic fluid is concentrated at room temperature by an air current, and when a volume of from 6 to 8 cc. has been reached the aqueous residue is injected into immature female rats weighing from 20 to 30 Gm. One hundred hours after the first injection the animals are killed, the ovaries sectioned and the amount of ovarian stimulation (manifested by the degree of follicle ripening) determined according to the standard described by Aschheim and Zondek.[22] Follicle ripening alone signifies anterior pituitary reaction I (prolan "A" effect, A P R I); blood spots signify A P R II; atretic corpora lutea A P R III (prolan "B").[18]

In the normal woman the greatest blood concentration is noted from six to nine days following the onset of the preceding menstruation. At this time as much as 25 rat units per liter (R. U. L.) of prolan A may be found. In a few instances a trace of the luteinizing factor (prolan B) has been noted.

PREPITUITARY MATURITY FACTOR TEST OF THE URINE

The prepituitary factor present in the urine is determined by the "concentration technic" described by Zondek[23] for the pregnancy test. We have found it of advantage to use 120, 100 and 80 cc. of acidified urine. To these amounts of urine four times their volume of 95 per cent alcohol is added. The prolan A and B are precipitated at this concentration, removed from the supernatant fluid by centrifugalization and freed from female sex hormone by washing with ether. The ether insoluble residue is dissolved in water and injected into immature mice.

Our data obtained from the urines are as yet incomplete.

By the preceding methods we are able to determine the female sex hormone level in the blood as well as the amount excreted in the urine.

An encouraging beginning for similar determinations of the prepituitary factor is under way. These results will be reported in a subsequent article.

Reichert, Pencharz, Simpson, Meyer and Evans[24] since this article was completed, have raised the question whether the maturity factor obtained from the prepituitary and the similar factor found in the urine of pregnant women, both called "prolan" by Zondek, are identical. His experiments show that the urinary "prolan" is ineffective after hyophysectomy. They further suggest[25] that the urinary "prolan" may be an activator of the inactive prohormone of the hypophysis and that possibly it converts the growth hormone into the gonad stimulating one.

CLINICAL APPLICATION OF THE HORMONE TESTS

Prepituitary.—The work along these lines has not as yet been sufficiently advanced to determine an absolute norm. Consequently no attempt has been made to draw conclusions from such abnormal cases as have been investigated. However, much evidence points to the fact that many of the ovarian functional disturbances eventually may be traced definitely to functional hypophyseal derangements.[18]

Ovarian Overfunction.—Puberty Bleeding: More than a dozen of these adolescents have now been followed for from six to three years. Both the clinical and the hormonal picture in every member of this group is alike. The abnormal bleedings may be of either the menorrhagia or the metrorrhagia type and eventually lead to grave exsanguination. In contrast to the abnormal functional bleedings of mature women, the blood hormone level for female sex hormone appears constantly high, so that an overloading of the circulation is demonstrated (fig. 4 *A*). Coincidentally the bleeding mucosa shows marked cystic endometrial hyperplasia. The urine excretion of these girls also demonstrates the marked overproduction of the hormone, as an undue amount is excreted constantly, often without typical cyclic variation.

Preclimacteric Bleeding: Climacteric bleeding of purely functional character likewise shows a high hormone blood level, but usually some cyclic variation is noted. The resulting endometrial changes strikingly resemble those of the puberty group although in most instances the myometrium appears to be simultaneously stimulated to hyperplasia (which, according to Teel,[26] is a prepituitary growth hormone effect).

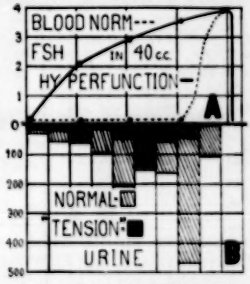

Fig. 4.—Graphs of blood and urine showing curve of female sex hormone: The blood represents the amount found in 40 cc.; the graph of the urine shows the total excretion in mouse unit hyperfunction. *A*, puberty and preclimacteric bleeding; dotted line shows normal function, solid line hyperfunction. *B*, urine of premenstrual tension: normal urine in shaded lines; "hypertension" due to underexcretion shown in solid black.

In another group, which I have named "premenstrual hypertension," the local genital symptoms may be absent, the entire clinical picture being dominated by the marked nervous and vascular symptoms preceding menstruation. These symptoms are explained by our hormone studies. In some instances the condition appears to be due to an overproduction of the hormone, as shown by the excessive amounts recovered premenstrually from the circulation (from two to three times normal), the excretion being normal (fig. 4 *A*). In other members of this group, I have gathered the impression that the overloading of the circulation is due to an underexcretion of the hormone, as the amount excreted during an entire cycle is less than half of that normally found in cyclic females[27] (fig. 4 *B*).

Maturity Menorrhagia and Metrorrhagia: Maturity menorrhagia and metrorrhagia has not been elucidated by our hormone studies. Occasionally a blood cycle can be demonstrated, apparently unaffected by the continuous bleeding. In the majority of cases, however, the blood tests prove negative throughout the cycle. Possibly, studies of the pituitary cycle may prove of value in determining the basis of these conditions. The endometrium may be at the normal resting stage, show

22. Aschheim, Selmar: The Early Diagnosis of Pregnancy, Chorioepithelioma and Hydatidiform Mole by the Aschheim-Zondek Test, Am. J. Obst. & Gynec. **19**: 335 (March) 1930.

23. Zondek, Bernhard: Zur Methodik der Schwangerschaftsreaktion aus dem Harn durch Nachweis des hypophysenvorderlappen Hormons, Klin. Wchnschr. **9**: 964 (May 24) 1930.

24. Reichert, F. L.; Pencharz, R. I.; Simpson, Miriam E.; Meyer, Karl; and Evans, H. M.: Proc. Soc. Exper. Biol. & Med. **28**: 843 (May) 1931.

25. Evans, H. M.; Meyer, Karl; and Simpson, Miriam R.: Proc. Soc. Exper. Biol. & Med. **28**: 845 (May) 1931.

26. Teel, H. M.: The Effect of the Growth Principle of the Hypophysis on the Female Genital Tract: With the Report of the Hypertrophic Changes in a Case of Acromegaly, Endocrinology **13**: 521 (Nov.-Dec.) 1929.

27. Frank, R. T.: The Hormonal Causes of Premenstrual Tension, Arch. Neurol. & Psychiat., to be published.

typical cyclic variations, or be of the stationary hyperplastic type.[28]

Underfunction.—The hormone tests have proved most instructive in the study of hypofunctional conditions. The two main complexes, roughly classified according to the most striking clinical symptom, include amenorrheas and sterilities. The hormone investigations have shown that these general groupings include a variety of conditions.

Amenorrhea: Among the amenorrheas, three main types can be recognized. The first consists of amenorrheas with a definite blood cycle which, however, never reaches normal levels and which, therefore, I have called a "subthreshold cycle."

(*a*) Subthreshold blood cycle. These patients at more or less regular intervals show an accumulation of hormone in the blood, which, however, rarely reaches beyond 2 +, which, in our studies, we consider the lower limit for positive reactions. Such patients usually also show a typical urine curve with increase of excretion at the time approximately coinciding with follicle ripening or ovulation, and another period which must

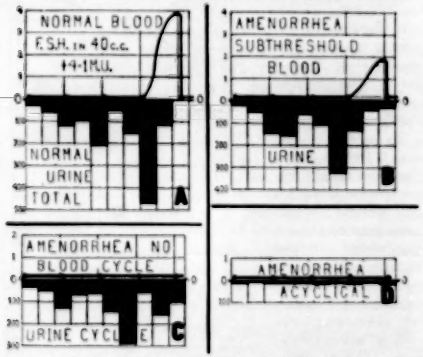

Fig. 5.—Graphs of specimens of blood and of urine showing curve of female sex hormone in the blood samples (40 cc.), as well as total mouse units excreted in the urine: *A*, normal fertile woman shown for comparison; *B*, amenorrhea (or sterility) with subthreshold blood cycle, and fairly normal urine cycle; *C*, amenorrhea without blood cycle but with urine cycle; *D*, acyclic amenorrhea.

be compared with the premenstrual time, although bleeding does not occur (fig. 5 *B*).

(*b*) Negative blood cycle. In these patients frequent and long continued blood examinations fail to demonstrate accumulation of hormone with the amount of blood investigated (40 cc.). On the other hand, an excess of hormone is found in the urine over long periods of observation. We have been forced to explain this condition as due to an abnormal permeability of the kidney, in other words, a low renal hormone threshold, which contrasts sharply with some "premenstrual tensions" in which the renal threshold is abnormally high (fig. 5 *C*).

(*c*) Acyclic amenorrheas. In these, neither the blood nor the urine shows demonstrable quantities of female sex hormone (fig. 5 *D*).

Clinically these groups are indistinguishable, good subthreshold blood cycles having been demonstrated in patients with absent vaginas who have never menstruated. On the other hand, in acyclic individuals, the amenorrhea may have existed for only a short period, and yet the prognosis is poor.

Sterility: In every case of sterility spoken of in this connection, semen studies of the husband have shown potency, and mechanical (tubal stenosis) as well as inflammatory causes could be excluded. Among this group only a small number show normal hormonal conditions.

The majority of menstruating sterile women either show a subthreshold blood cycle (fig. 5 *B*), such as was described under amenorrheas, or negative blood conditions with urinary cycle present (fig. 5 *C*). Those cases in which sterility is combined with amenorrhea are explained by the hormonal changes accompanying the amenorrhea.

In the sterile types, also, the grouping and prognosis depends almost exclusively on the hormonal observations. However, as our experience has increased, stigmas noted in the individuals in whom these various hormonal changes have been studied enable us to predict with some degree of assurance what hormonal deviations may be expected. Lack of space prevents me from enlarging on this important phase of our investigations.

A generalization based on these hormone studies makes it evident that circulatory hormonal overcharge may result either from overproduction of the hormone or from hormonal underexcretion. In an analogous way, an undercharged circulation may be due to underproduction, overexcretion, or cessation of function.

Therapy.—With the preceding observations in mind, I feel justified in concluding that the present methods of therapy are not only illogical but in many instances scandalous. Some may be unaware of the widespread prevalence of dosing patients with inert commercial products. The point has been reached at which physicians, who in other disciplines of medicine are scrupulous, careful and sane, in this field prescribe ready made products solely characterized by number, containing heterogeneous mixtures of inert substances which include all but the hoof and hide of our domestic animals.

While such products as thyroid substance, insulin and parathyroid produce striking and concordant results in appropriate cases, the opposite applies even to the few potent extracts used in the genital sphere.

Our hopes have been dashed because of the fact that the potent female sex hormone does not cause the anticipated therapeutic results. This is fully explained since we recognize that this now purified substance acts solely on the tubular tract and, according to competent testimony,[29] when given in large doses over long periods, eventually causes sclerosis of the ovaries.

My investigations with all the supposedly potent anterior lobe preparations commercially obtainable have proved negative, as has also been found by Jannsen.[30] Attempts to utilize the high prepituitary hormone titer of pregnancy blood by means of transfusion appears nullified by the complete and rapid excretion noted by Erhardt.[31]

28. Frank, R. T.: Gynecological and Obstetrical Pathology, ed. 2, New York, D. Appleton & Co., 1931.

29. Kunde, M. M.; D'Amour, F. E.; Gustavson, R. G., and Carlson, A. J.: Effect of Estrin Injections on Reproductive Organs, Hypophysis, Kidney, Adrenals, Thyroid and Blood Vascular System, Proc. Soc. Exper. Biol. & Med. **29**:122 (Nov.) 1930. Hauptstein, P.: Zum Wirkungsmechanismus des Sexual (Follikel) Hormons, Endokrinologie **8**:169, 1931. Leonard, S. L.; Meyer, R. K., and Hisaw, F. L.: The Effect of Oestrin on Development of the Ovary in Immature Female Rats, Endocrinology **13**:16; **15**:17 (Jan.-Feb.) 1931.

30. Jannsen: Verhandl. d. Deutsch. Gesellsch. f. inn. Med., 42d congress, 1930, p. 82.

31. Erhardt: Transfusion of Pregnancy Blood, Verhandl. d. Deutsch. Gesellsch. f. inn. Med. 42d congress, 1930, p. 87.

My associate, Dr. S. H. Geist, recently reported (at the last meeting of the American Gynecological Society) the negative results, as checked up by ovaries removed at operation, produced by as large a dosage as 1,500 rat units of the supposedly active prepituitary luteinizing factor.

My own efforts at therapy therefore have been directed toward influencing the underlying disturbances of the ovarian function by indirect means.

The Treatment of Overcharge (Hyperfunction): Our studies of puberty menorrhagia and metrorrhagia have convinced us that these conditions are usually self-limited or, as the older type of physician would have described it, are eventually outgrown. I therefore place these patients in the best surroundings available, at rest, with roborant diet, fresh air and sunlight. Not infrequently one or more curettages are necessary to relieve the bleeding temporarily. Transfusion may have to be practiced repeatedly. In several instances, two of my associates have resected the ovaries with good results, although at least two relapses have been noted. In two patients it has been necessary to give a reducing dose of x-rays almost to the point of amenorrhea. These two girls are now menstruating normally.

Injection of parathyroid, of insulin and of theelin, as well as large doses of calcium, have proved unavailing in our hands in this type of case.

The Bleedings of Maturity: The bleedings of maturity have likewise not responded to endocrine therapy. Here less hesitation has prevailed in employing the ordinary methods available to the gynecologist, such as curettage and roentgen therapy, as a majority of these patients have already borne numerous children.

In the preclimacterium, bleeding has been controlled by curettage, roentgen therapy or, in rare instances, the intra-uterine application of radium.

In the cases of "premenstrual tension" the overcharged circulation did not produce excessive bleeding. Renal (theobromine sodiosalicylate, caffeine) and intestinal elimination (salines) and limitations of fluids, combined with calcium therapy, has relieved a number of patients.

Undercharge (Hypofunction): A number of cases of amenorrhea have been found to be only secondarily due to ovarian disturbances. These include the symptomatic amenorrheas noted in tuberculosis, change of climate or secondary to other endocrine diseases, especially those of hypophyseal and thyroid origin. In these cases the underlying disease or condition, when amenable to treatment, has been attacked. Amenorrhea due to malnutrition, usually accompanied by moderate diminution in the basal metabolic rate and frequently mistaken as due to thyroid underfunction, responds in a gratifying fashion to a high protein diet.

I have been unable to influence the amenorrheas resulting from marked ovarian underactivity and in most instances have advised against the so-called stimulating dose of x-rays now advocated by some. The use of x-rays is never justified unless preliminary studies have demonstrated the presence of a subthreshold blood cycle, as otherwise already inert ovaries are completely destroyed from a functional standpoint. I have seen a number of cases in which irreparable damage has resulted from roentgen therapy applied for the relief of amenorrhea.

Taking for granted that the husband has been found potent and that inflammatory and mechanical causes, which so often coincide, have been fully excluded, the several varieties of sterility require different treatment. Most readily recognized among these groups are the constitutionally handicapped in which evidence of advanced infantilism, both local and general, proves that the genital organs have never been fully developed. When the thyroid function is markedly depressed, and unfortunately this group is small, thyroid medication is of sovereign value. We have reason to suspect that some of the sterilities are due to prepituitary functional disturbances, but the data at hand are as yet too scanty to be of convincing value. Great success is obtained by all, in the group of cases in which the sterility is transitory. Here wonderful and brilliant therapeutic results are recorded from every source. However, I have a large number of case histories available in which nothing whatever was done and fertility developed. In this group sex hygiene, dietary supervision (although I do not believe that the lack of vitamins plays any considerable rôle in the well fed human being), and reassurance of the patient are as effective as any therapy yet devised.

The climacteric symptoms, whether due to artificial or to the natural menopause, appear to result from a lack of female sex hormone in the circulation and an excess of prepituitary maturity factor as demonstrated by Zondek.[32] The results following the use of theelin—this appears to be its most useful field—have been too variable to be convincing. This product probably acts on the hypophysis by causing some regression of the pituitary castration changes. In my hands thorough elimination, in severe instances occasional venesection, and calcium in high dosage have proved as effective as female sex hormone therapy.

10 East Eighty-Fifth Street.

THE RÔLE OF PROGESTIN IN THE FEMALE REPRODUCTIVE CYCLE*

GEORGE VAN S. SMITH, M.D.
AND
O. WATKINS SMITH, PH.D.
BROOKLINE, MASS.

The term "progestin" was applied by Allen[1] and by Corner to the hormone of the corpus luteum, which maintains in a normal state of pregnancy rabbits castrated the day after mating. In experimental work, progestin has been found to produce most of the effects already known to be associated with the functioning corpus luteum. These functions are characteristic proliferation of the endometrium for the nourishment and implantation of ova, growth of the decidua, maintenance of pregnancy and inhibition of ovulation. Excess of progestin, by raising the threshold of uterine muscle by stimulation, has been shown to inhibit the delivery mechanism, with consequent death of pregnancy in utero. In addition, we have found[2] that progestin, through stimulation of the suprarenal glands, may have

32. Zondek, Bernhard: Ueber die Hormone des Hypophysenvorderlappens: II. (Follicle Ripening Hormones—Prolan A), Klin. Wchnschr. **9**: 393 (March 1) 1930.

* From the Fearing Research Laboratory, Free Hospital for Women.
* This work was facilitated by the aid of the Mrs. William Lowell Putnam Investigation of the Toxemias of Pregnancy, and the support also of Mr. Reginald W. Bird.

* Read before the Section on Obstetrics, Gynecology and Abdominal Surgery at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 11, 1931.

* Through the hearty cooperation of Dr. John Rock, the Boston Lying-In Hospital and Dr. Frank A. Pemberton, the clinical application of the luteinizing hormone has been thus far made possible.

1. Allen, W. M.: Am. J. Physiol. **92**: 174 (Feb.) 1930.
2. Smith, G. V., and Watkins, O.: Am. J. Physiol. **94**: 586 (Sept.) 1930. Watkins, O., and Smith, G. V.: Am. J. Physiol. **96**: 28 (Jan.) 1931.

other functions, both metabolic and vasomotor. In the course of this paper another activity of progestin, in relation to the excretion of the ovarian follicle hormone, will be presented. Since the anterior portion of the hypophysis contains a hormone which stimulates growth of the corpus luteum, it is assumed with much supportive evidence that the production of progestin is conditioned by the presence of this luteinizing hormone.

In the human menstrual cycle the progestin secreted by the active corpus luteum following ovulation normally prevents further ovulation and brings about the characteristic premenstrual, secretory changes in the endometrium, the ovarian follicle hormone, estrin or folliculin, being a necessary factor in this process. The decrease in progestin toward the end of the cycle is followed by menstruation. To account for the rise and cadence of the corpus luteum and the concomitant variations in progestin, it is necessary, for the present, to postulate that when the graafian follicle reaches a certain stage in its growth under the influence of the gonad-stimulating hormone of the anterior hypophysis there takes place increased hypophyseal activity, with consequent ovulation and luteinization. Further, since progestin inhibits ovulation and also inhibits the action of pituitary transplants in causing maturity in rats,[3] it apparently depresses the pars anterior. It may be, therefore, that the regression of the corpus luteum is due to depression of the pars anterior by progestin.

Fertilization of the ovum is the normal occasion for survival of the corpus luteum and the continued action of progestin, which prevents menstruation and causes increased proliferation of the endometrium, sensitizing it for implantation of the ovum and decidual formation. This situation accompanies the appearance in the blood and urine of large amounts of the luteinizing hormone, the production of which is taken over from the anterior hypophysis by the trophoblast and later by the placenta. Although death of pregnancy in experimental animals follows the removal of progestin by ablation of the corpus luteum, in human beings pregnancy has been known to progress normally after early ovariectomy. Apparently, progestin is not a necessary factor for survival of pregnancy once placentation has occurred. This point is further borne out by the well known regression of the corpus luteum after the middle of gestation. In this connection some factor other than decrease of the luteinizing hormone must be sought to explain the regression of the corpus luteum in late pregnancy, for there is still much luteinizing hormone so long as the placenta survives. On the same basis, some factor other than progestin must account for the usual inhibition of ovulation in later pregnancy and lactation.

Although menstruation normally follows on the withdrawal of progestin, Hartman's[4] work on monkeys would indicate that the flowing is actually the positive effect of anterior pituitary activity in the presence of the folliculin accumulated during the previous cycle. It has already been stated that the follicle hormone is necessary for the endometrial proliferation caused by progestin. Thus folliculin, produced under the influence of the gonad-stimulating hormone of the anterior hypophysis, and progestin, produced under the influence of the luteinizing hormone of the same gland, are both synergistic and antagonistic. In their simplest form some abnormal conditions in the female reproductive phases are due to a lack of balance between these four factors. For example, insufficient gonad-stimulating activity by the pars anterior or inadequate ovarian response would make for amenorrhea or scanty menstruation and sterility. Evidence of this insufficiency is the genital hypoplasia so common in these cases, indicating too little follicle hormone, one of whose functions is to cause uterine and vaginal growth. Further, an abnormally persistent corpus luteum would also account for sterility and amenorrhea. This situation simulates the condition of pseudopregnancy as seen in animals. Administration of the gonad-stimulating hormone is indicated under these circumstances to override the corpus luteum, but as yet no potent preparation for clinical use has become available. The follicle hormone has been tried quite extensively, with only slightly encouraging results. We have used it in the form of theelin [5] and a crude but potent extract of urine from pregnant women, with partial and uncertain benefit. Giving this hormone alone would not be expected to remedy these conditions unless it activated the anterior hypophysis, but definite evidence of this is lacking. On the other hand, sterility might follow if the anterior hypophysis were too active, overriding progestin and causing menstruation before the fertilized ovum could become implanted.

By the same process of reasoning, abnormal menstruation may result from excessive activity of the gonad-stimulating hormone or excessive follicular response or from insufficient production of the luteinizing hormone or inadequate supply of progestin from the corpus luteum. Although, undoubtedly, other endocrine and constitutional factors are involved, administration of the luteinizing hormone or progestin is indicated. There is still no clinical preparation of progestin. We have given intramuscularly in various doses the luteinizing hormone, prepared from the urine of pregnant women by the method of Evans.[6] To date, eight patients with too frequent and excessive menstruation have been treated, causes for flowing other than endocrine having been eliminated. All were definitely relieved; one of these had dysmenorrhea also and was relieved. It is interesting that one patient complained of hot flushes following treatment. The luteinizing hormone failed to stop the flowing in a case of fibroids. Three other cases have been treated, with relief: a case presenting nausea and fainting spells at the time of menstruation, a case of pelvic inflammation with flowing, and a case of endometriosis with pain and flowing, unrelieved by previous conservative operation. It is still too soon to regard these early results as more than hopeful, but they indicate beneficial results following administration of the luteinizing hormone, either through a direct effect or through stimulation of progestin.

On the same basis, it was reasoned that insufficient progestin, by failing to maintain the decidua and thus impairing the vitality of the ovum, might be a factor in miscarriage. Seven other patients, from two to six months pregnant, were given the luteinizing hormone in total doses of from 50 to 100 cc. over periods ranging from five to twenty days. Of these, four were flowing, two were flowing and vomiting, and one was vomiting. All were managed clinically as cases of threatened miscarriage. In six, all flowing and vomiting ceased within ten days. The seventh patient had a marginal placenta praevia and was delivered. Three patients have since

3. Hisaw, F. L.; Meyer, R. K.; Fevold, H. L., and Leonard, S. L.: Anat. Rec. 44: 205, 1929.
4. Hartman, C. G.; Firor, W. M., and Geiling, E. M. K.: Am. J. Physiol. 95: 662 (Dec.) 1930.

5. The Doisy crystalline preparation supplied by Parke, Davis & Co.
6. Parke, Davis & Co. and Dr. E. A. Sharp of that company cooperated in supplying us with this and other preparations.

miscarried. The other three are getting along normally from two to six weeks after treatment. No conclusions can yet be made as to clinical results.

For the present our chief interest centers in the change of endocrine balance in these pregnant patients following the administration of the luteinizing hormone. We have studied the folliculin of the blood and the urine by the Allen-Doisy rat test. A number of the patients had markedly high folliculin levels as compared with normal patients at the same stage of gestation. The blood regularly showed a decrease in folliculin, five or more days after the start of treatment. Having first satisfied ourselves that the amounts of folliculin in different specimens of urine can be compared satisfactorily in terms of urinary creatinine, we found that all these patients had definitely less folliculin in the urine when it was tested after from five to nineteen days of treatment. As a control, three of these patients were not given the luteinizing hormone until after a week of miscarriage routine, during which time there was no folliculin change.

This finding led us to study folliculin excretion in rabbits. We are using urinary creatinine again as a means for obtaining comparable results and are also measuring the twenty-four hour urine output for calculating total excretion. Preliminary experiments thus far indicate the following: Injection of large doses of theelin in normal and spayed doe rabbits results in only a little excretion, less than 10 per cent of the amount given. If luteinizing hormone is given before and with theelin, the normal rabbits show strikingly increased folliculin excretion, but the spayed rabbits do not show any increase. If progestin is given before and with theelin, there is a 50 to 75 per cent recovery in the urine in both normal and spayed animals.

These experiments show that progestin has another function; namely, that of promoting excretion of folliculin. Further evidence of this was found in one of the pregnancy cases mentioned in which the urinary folliculin was determined the day after the first injection. It was increased. By the tenth day it had decreased markedly. Since the folliculin in the urine as well as the blood of these patients decreased following continued administration of the luteinizing hormone, we have, in this, additional evidence of an inhibitory influence of progestin on the actual production of folliculin.

Although the clinical results of giving luteinizing hormone in early pregnancy are still too few to be used as a basis for any conclusions, we feel that the finding of marked drops in the folliculin level after treatment, together with the experimental discovery of the effect of progestin on folliculin excretion, indicates actual physiologic reactions which may in time have valuable clinical application.

SUMMARY

1. The functions of progestin and its rôle in the normal human menstrual cycle and in pregnancy have been briefly outlined within the limits of our present knowledge.

2. The luteinizing hormone which stimulates the production of progestin has been administered, with promising results, to nineteen patients whose chief symptom was abnormal flowing.

3. Early clinical and experimental evidence points to another function of progestin; namely, that of inhibiting the production of the follicle hormone and promoting its excretion.

Free Hospital for Women.

THE HYPOPHYSEAL-OVARIAN RELATIONSHIP

QUANTITATIVE STUDIES WITH ESPECIAL REFERENCE TO HYPERPLASIA OF THE ENDOMETRIUM *

JOHN C. BURCH, M.D.
W. L. WILLIAMS, M.D.
J. M. WOLFE, PH.D.
AND
R. S. CUNNINGHAM, M.D.
NASHVILLE, TENN.

Endometrial hyperplasia has long been one of the major problems of gynecology. Its exact etiology has been unknown, but its relationship to a disordered ovarian function has been recognized.

The material presented in this paper is taken from studies carried out on the etiology of endometrial hyperplasia [1] and on the functional relationship between the hypophysis and the ovary.[2] These studies suggest that certain disorders of the hypophyseal-ovarian relationship may have considerable importance in our understanding of endometrial hyperplasia.

In applying the results of animal experiments to the interpretation of conditions in human beings, much confusion has arisen on account of differences in terminology as applied to the estrual and the menstrual cycles.

Allen [3] has accurately described the estrual cycle of the mouse. The unmated mouse has a period of estrus every four to five days. This period is characterized by cornification of the vaginal epithelium. Ovulation takes place during the latter part of the estrual phase, but the corpus luteum remains inactive unless the animal is allowed to copulate. If copulation takes place with a vasectomized buck, a stage of pseudopregnancy results. This stage of pseudopregnancy corresponds to that phase of the human menstrual cycle lying between the fourteenth and the twenty-eighth days.

Two or three days before the onset of estrus in the mouse, the epithelium becomes markedly active, the gland cells multiply, and numerous mitotic figures are present. There is definite pseudostratification of the epithelium, and a fair amount of secretion is found in the glands. There is edema of the stroma. During pseudopregnancy the gland cells lose their pseudostratified appearance and become more regular. No mitoses are present, and there is some enlargement of the stroma cells. In the mouse, therefore, there are two distinct phases; one before ovulation and one after.

In the human being, following the cessation of the menstrual period, the uterine epithelium is of low columnar type. There are no mitoses and no secretion in the glands. The stroma is moderately edematous. After a few days the gland cells multiply, mitoses are present, and the mucosa increases in thickness. The edema becomes somewhat more prominent.

* From the Department of Obstetrics and Gynecology and the Department of Anatomy, Vanderbilt University School of Medicine.
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* Read before the Section on Obstetrics, Gynecology and Abdominal Surgery at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 11, 1931.

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3. Allen, Edgar: The Estrus Cycle in the Mouse, Am. J. Anat. **30**: 297-371 (May) 1922.

Following ovulation, the corpus luteum is formed. In the human being this structure functions irrespective of the act of copulation. In the uterus at this time (from sixteen to twenty-two days after the cessation of menstruation) numerous tufts or papillae project into the glands. The nuclei of the epithelial cells assume a more central position. There are no mitoses and there is no pseudostratification. The stroma cells increase in size and form a compact layer in the upper portion. Later, around the twenty-fifth day, the edema becomes quite marked. From this brief description it can readily be seen that the changes occurring in the human being are very similar to those found in the mouse.

The ovary has two known secretions, one first observed by Frank [4] and later studied more fully by Allen.[5] This has usually been called the "female sex hormone." In our opinion, it is more aptly designated as "estrin." Allen and Corner [6] have isolated another hormone, derived from the corpus luteum, which, when injected into rabbits, causes changes similar to those found in pseudopregnancy. By means of this extract of the corpus luteum, Allen and Corner have further been able to maintain pregnancy after the removal of the ovaries. Frank [4] has also shown that the estrus-producing hormone can be found in detectable amounts in the blood of human beings, beginning on the fourteenth day and increasing until menstruation.

It is fairly clear, then, that the changes preceding ovulation are the result of the estrous hormone and that the changes following ovulation are the result of the combined action of these two hormones. It is from this point of view that we have approached the problem of interpreting hyperplasias. These conditions have been thought to be the result of an ovarian dyscrasia, but it has not previously been possible to determine the type of this dyscrasia from the curettings.

Schroeder,[7] Shaw [8] and Graves [9] have all noted that, in their cases of Swiss cheese hyperplasias, no corpora lutea were found and that the ovaries were cystic. From this work the logical inference is that hyperplastic changes are the result of the unopposed action of estrin. We [1] have been able to confirm this hypothesis by comparing specimens of hyperplasia with the endometrium of spayed mice which had been injected with extracts of estrin and of corpus luteum and with a combination of the two. From these comparisons it was possible to demonstrate specific histologic pictures characteristic of each hormone.

Sections from twenty-eight cases of Swiss cheese hyperplasia were studied in the light of these comparisons and were found to be quite similar in many respects to the normal human endometrium of the sixth to the fourteenth day and to the endometrium of a mouse which had been injected with estrin. The Swiss cheese pattern is one of the most striking features of human hyperplasia but is not, in our opinion, of as great significance as the more minute changes of stroma edema, glandular pseudostratification and epithelial mitoses which are common in the estrin phase of the normal human cycle, in hyperplasia of the endometrium and in spayed mice injected with estrin. We have also observed two cases of typical Swiss cheese hyperplasia in which the ovaries contained no corpora lutea but did contain cysts of the graafian follicles. The fluid from these cysts was injected into spayed animals with the production of estrus. The endometrium of these experimental animals was quite similar to that seen in the respective human cases from which the fluid was obtained. From these observations we feel that it is legitimate to conclude that hyperplasia of the endometrium results from an unopposed action of the estrus-producing hormone.

The easiest and simplest explanation of an unopposed action of estrin is that the patient has failed to ovulate, since without ovulation there can normally be no corpora lutea. This failure to ovulate may be due to a breakdown in the inherent mechanism of ovulation or to simple mechanical conditions, such as inflammatory thickening of the tunica albuginea or to dense adhesions. These conditions prevent rupture of the follicles.

It has long been thought probable that some other organ played a part in the ovarian cycle. Experimental evidence of this was presented independently in 1927 by Smith and Engle [10] and by Zondek and Aschheim.[11] These changes have been confirmed repeatedly. Ovulation was a variable feature of the phenomena. Friedman [12] has shown by transplantation experiments that ovulation is the result of some humoral mechanism. Knauer [13] had previously come to the same conclusion. Fee and Parkes [14] hypophysectomized rabbits within one hour after copulation and found that ovulation did not occur. In connection with this experiment it should be borne in mind that the rabbit does not ovulate spontaneously but only after copulation. Smith and Engle [15] found that anterior hypophyseal tissue taken from guinea-pigs in the estrous period had relatively little capacity to increase the size of the ovary, while glands taken from animals in diestrus were more potent in this regard. These observations suggested that there might be a variation in the amount of the hormones secreted by the anterior lobe of the hypophysis during the different phases of the estrual cycle.

This contention was further strengthened by a series of experiments carried out in this laboratory.[16] Female rats were divided into experimental and control groups. The animals of both groups were spayed two weeks before the specific experiments were carried out. The animals in the experimental group received a series of six subcutaneous injections of an alcoholic extract of human placenta (given at twenty-four-hour intervals). The hypophyses of the animals of each group were transplanted into immature female mice as test animals. The ovaries of the mice receiving anterior lobe tissue from the injected rats were much larger than those

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6. Allen, W. M., and Corner, G. W.: Physiology of the Corpus Luteum: III. Normal Growth and Implantation of the Embryos After Very Early Ablation of the Ovaries, under the Influence of Extracts of the Corpus Luteum, Am. J. Physiol. **88**: 340-346 (March) 1929.

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12. Friedman, M. H.: The Mechanism of Ovulation in the Rabbit: I. Demonstration of the Humoral Mechanism, Am. J. Physiol. **89**: 438-442 (July) 1929.

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14. Fee, A. R., and Parkes, A. S.: Studies on Ovulation: I. The Relation of the Anterior Pituitary Body to Ovulation in the Rabbit, J. Physiol. **67**: 383-388 (July) 1929.

15. Smith, P. E., and Engle, E. T.: Evidence of a Correlation Between the Amount of Gonadal Stimulating Hormone Present in the Pituitary of the Guinea-Pig and the Stage of the Reproductive Cycle, Anat. Rec. **46**: 38 (March) 1929.

16. Burch and Cunningham (footnote 2).

receiving anterior lobe substance from the control group. The ratio was 5 to 2.

To further test this concept of a variation in the hormones produced in the hypophysis, concurrent with the normal estrual cycle, a large number of experiments have been carried out on the capacity of the anterior hypophysis of the sow to produce ovulation in the normal sexually mature rabbit.[17] The work of Corner [18] on the estrual cycle of the sow was used as a basis for the selection of the donors. The material was selected on the killing floor of a local abattoir and brought immediately to the laboratory. The hypophysis was removed and the anterior lobe dissected out and carefully weighed. It was then crushed in physiologic solution of sodium chloride and ground up with sterile sand. The mixture was centrifugated for thirty minutes and the supernatant fluid drawn off. This was diluted to the point at which 1 cc. represented 5 mg. of the fresh tissue. This fluid was injected in varying amounts into the marginal ear vein of sexually mature female rabbits. It is obvious that the fluid did not contain as much tissue as we have calculated, but a constant technic has been used and whatever error was present has been the same in all experiments. The rabbits injected either were killed or had the ovaries examined by laparotomy within from twenty-four to thirty hours after the injection. When the hypophysis was taken from a sow in proestrus, an amount of the suspension representing 1 mg. induced ovulation in a rabbit. Ten milligrams of anterior lobe tissue was necessary to induce ovulation when the donor sows were in heat. Forty milligrams was required to induce ovulation when the ovaries of donor sows contained active corpora lutea. These results indicate a definite cyclic variation in the capacity of the anterior lobe to produce ovulation.

The evidence reviewed in the foregoing indicates that estrin is probably the direct etiologic factor in the production of endometrial hyperplasia. This effect could result either from the presence of an excessive amount of their hormone or from the absence of some substance or mechanism which normally holds its action in check. It seems to us that the hormone produced by the corpus luteum is the agent which is most likely to be responsible for this action; this seems especially pertinent since the ovaries from cases of hyperplasia have been found to be uniformly lacking in corpora lutea. It should further be noted that the failure in ovulation (which obviously results in absence of corpora lutea) could well be due to some interference with the normal activity of the hypophysis. This could be either a deficiency in the substance producing ovulation or a failure in its release or utilization.

SUMMARY

Our experiments tend to show that endometrial hyperplasia is due to a relative excess of estrin. This of course can result from either an actual excess or a relative excess. The latter seems more probable. The ovary and the hypophysis are closely associated and each affects the other. There is a definite cyclic variation in the capacity of the anterior hypophysis to produce ovulation. Variations and deficiencies in the ovulation cycle might easily cause alterations in the menstrual cycle with idiopathic bleeding as a symptom.

2112 West End Avenue.

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18. Corner, G. W.: Cyclic Changes in the Ovaries and Uterus of the Sow, and Their Relation to the Mechanism of Implantation, Contrib. Embryol. **13**: 117-146, 1921.

THE EFFECT OF HYPOPHYSECTOMY ON OVULATION AND CORPUS LUTEUM FORMATION IN THE RABBIT *

PHILIP E. SMITH, PH.D.
AND
W. E. WHITE, M.A.
NEW YORK

That the secretion of the anterior pituitary is essential to gonadal function seems to be one of the most firmly established facts in the physiology of the reproductive system. With ablation of the anterior pituitary, follicles cease to develop and those with cavity formation undergo atresia. The uterus and vagina decrease in size and their cyclic changes cease. In the male the effects are equally pronounced. Pituitary implants restore gonad activity. In immature rats and mice, pituitary administration precociously develops the reproductive system, and in adults past the menopause it will induce estrus.

Some recent work has shown that the pituitary sex hormone (or hormones) is secreted into the body fluids with almost amazing rapidity. This work at the same time has raised a question regarding the essentiality of the anterior pituitary in stimulating the growth of the corpus luteum. These results are so striking that we deemed it worth while to repeat and extend the experiments, with a somewhat altered technic. The results obtained form the basis for this paper.

The work to which we refer is that reported in a series of papers by Fee and Parkes [1] in rabbits. This form, as first shown by Heape,[2] a finding which has been repeatedly confirmed, does not ovulate spontaneously but only after mating or other sexual excitement and then within a period of from ten to twelve hours. Fee and Parkes, with a technic which they have ventured to characterize as hypophysectomy, decerebrated a series of rabbits at varying periods after mating, dissected out the pituitary in part of the animals and left it in situ in others. Ovulation took place only if the pituitary was left in place for a period of an hour (approximately) or longer. According to these findings, then, the pituitary, which had been secreting at a rate only sufficient to bring about a development of the follicles to the condition obtained in the nonmated estrus rabbit, by coitus was stimulated to secrete within the period of one hour sufficient gonad-stimulating hormone to bring about the maturation of the follicles. More surprising still was the observation that in the animals the development of the corpora, although somewhat slowed, nevertheless was normal in character for a period of thirty-six hours after copulation. Longer periods of observation were not reliable and seldom possible because of the severe general effects of the decerebration. These investigators carefully stated that this period of growth of the corpora did not show that their further development could take place independently of the pituitary; nevertheless the results suggest this possibility.

* From the Department of Anatomy, Columbia University College of Physicians and Surgeons.
* Aided by a grant from the Committee for Research in Problems of Sex of the National Research Council.
* Read before the Section on Obstetrics, Gynecology and Abdominal Surgery at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 11, 1931.

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2. Heape, W.: Ovulation and Degeneration of the Ova in the Rabbit, Proc. Roy. Soc. **76**: 260-267, 1905.

In our hypophysectomies we have not used a technic which subjects the animals to a severe trauma, such as does decerebration, but one which leaves them in an essentially healthy condition. It seems unnecessary to describe the operative procedure in detail. It will suffice to state that an oral approach through the soft palate is used. The capacious blood sinus in which the pituitary lies, surrounded by its dense capsule, is injected with warm bone wax. The capsule is then exposed and opened, and both lobes of the pituitary are removed with a cannula and negative pressure. It is not a blind operation, all essential structures being visible. There is little bleeding. The animals show a good recovery and usually remain in excellent condition. Ten successful operations have been performed and the total removal of the anterior and posterior pituitary confirmed by a study of serial sections of the contents of the sella. Periods of from one and a quarter to seventeen hours elapsed between mating and the actual removal of the pituitary. In each of seven of the animals, both ovaries were inspected and one of them was removed for sectioning about twenty-four hours after hypophysectomy, the second ovary being removed twenty-four hours later. In each of two of the animals, one ovary was removed four days and the other eight days after the hypophysectomy. In every case, ovulation occurred, even though the pituitary was removed within an hour and a quarter after the mating. Since follicular growth and maturation will not take place in the absence of the pituitary gonad-stimulating hormone, it is evident that the stimulus afforded by copulation has caused, by some at present unknown mechanism, an immediate and considerable discharge of this hormone. This response is striking and gives a conception of the anterior pituitary as a secretory-labile and responsive structure, which in spontaneously ovulating forms, prior to ovulation, may pour out its stored secretion by some releasing mechanism.

The second phase of our study concerns the essentiality of a pituitary secretion for the complete development and function of the corpus luteum. Our work confirms the observation of Deanesly, Fee and Parkes that corpus luteum formation takes place in rabbits even though the pituitary has been removed but a short time after mating and, consequently, several hours before ovulation has taken place. The corpora in such animals twenty-four hours after hypophysectomy (from fifteen to thirty hours after ovulation) appear to be normal, nor is there a slowing in the rate of development compared with unoperated controls, as noted by the previously named investigators. This is probably due to the fact that our operation left the animals in excellent condition, whereas their procedure led to the death of the animal within a period of from one to two days. Even in the ovaries removed at the end of the second day after hypophysectomy, or from fifty to fifty-five hours after mating, the corpora show no striking developmental failure as compared with the normal controls.

The lutein cells are large and typical in appearance, though apparently not quite as numerous as in the controls. The corpora have consequently a somewhat larger central cavity.

In the two animals in which the left and right ovaries were removed four and eight days, respectively, after hypophysectomy, the corpora show, however, a contrast with the normal. In those removed after a period of four days it is evident that little growth beyond that of the second day has taken place. Although there are many normal appearing lutein cells present, they are not as numerous as in the controls, and the central cavity is consequently much larger. The number of connective tissue cells in proportion to the lutein cells is much greater than normal. In the ovaries removed eight days after hypophysectomy the corpora have regressed. They appear avascular and small. They contrast markedly with the normal, which is larger and highly vascular and in which there remains but a remnant of the central cavity.

It is thus evident that after hypophysectomy the corpora will develop with little or no deviation from the normal for a period of approximately two days. They undergo this development without any postovulatory secretion of the hypophysis. Furthermore, since most of the animals were virgins, there is no possibility of any postovulatory pituitary secretion being still present from previous ovulation. That they will not undergo complete development under these conditions, however, is evident from the ovaries removed at four and eight day periods.

In order to see the effect on the completely formed corpora, a twenty-two day pregnant rabbit was hypophysectomized, one ovary being removed four days and the other eight days later. This animal aborted some of the fetuses on the third to the fourth days. When a laparotomy was performed on the fourth day, there were three dead fetuses in the uterus. The corpora, which have been shown to be essential to gestation in experimental animals, in this rabbit showed avascularity and regression when the animal was opened on the fourth day. So far as can be demonstrated by a single experiment, it is apparent then that the secretion of the anterior pituitary is essential for the functional maintenance of the corpora. Their regression may be primarily responsible for abortion which follows pituitary ablation.

COMMENT

In view of the well known effect of certain extracts (alkaline) of the hypophysis on the formation and maintenance of corpora lutea,[3] it is not surprising that complete development of the corpora failed in the absence of the hypophysis. The finding that they would develop for a period in excess of two days in the absence of any postovulatory secretion of the hypophysis was unexpected. That such is the case would seem to have some bearing on the problem of whether the anterior pituitary secretes only one or more than one hormone which act on the ovarian constituents. This problem has invariably been considered and its experimental solution attempted by noting the effects of the administration of pituitary implants or of extracts which have been made in different ways. Some of this work will be briefly mentioned. In work reported earlier by one of us,[4] it was found that injections of a saline supension of beef hypophyses prevented the restorative effects of implants on the ovaries and testes of hypophysectomized rats. Later, Evans and Simpson[5] reported that such injections prevented the

3. Evans, H. M., and Long, J. A.: Characteristic Effects on Growth, Estrus and Ovulation Induced by the Intraperitoneal Administration of Fresh Anterior Hypophyseal Substance, Proc. Nat. Acad. Sc. **8**: 38-39, 1922. Teel, H. M.: The Effects of Injecting Anterior Hypophyseal Fluid on the Course of Gestation in the Rat, Am. J. Physiol. **70**: 170-183 (Dec.) 1926. Shelesnyak, M. C.: The Production of Placentomata in Young Rats Following Gonadal Stimulation with Pituitary Implants, Am. J. Physiol. **95**: 387-393, 1931.

4. Smith, P. E.: The Disabilities Caused by Hypophysectomy and Their Repair, J. A. M. A. **88**: 158-161 (Jan. 15) 1927; Hypophysectomy and a Replacement Therapy in the Rat, Am. J. Anat. **45**: 205-273 (March) 1930.

5. Evans, H. M., and Simpson, Miriam E.: Antagonism of Growth and Sex Hormones of the Anterior Hypophysis, J. A. M. A. **91**: 1337 (Nov. 5) 1928.

stimulating effects of implants in immature rats. The latter investigators, because of these findings, postulated an antagonism between the gonad-stimulating and the growth hormones. The latter, they believed, carried the luteinizing factor. Engle [6] has shown that there are characteristic differences between the effects of injection of the urine of pregnancy with its anterior pituitary-like principle and of implants. Work on the purification of extracts has strengthened the idea of the duality of the pituitary sex hormone, especially the recent paper by Fevold, Hisaw and Leonard [7] and the work of Zondek.[8]

Although the data up to the present seem insufficient and the field not thoroughly enough explored to justify dogmatizing on the question of the unity or duality of the pituitary sex hormone, nevertheless there appears to be a definite trend toward the belief that there are two sex hormones secreted by the anterior hypophysis, one stimulating follicular growth, the other luteinization. The skeptics have been as yet satisfied to express their doubts in other ways than by publication. The purpose of introducing the subject here is to emphasize another angle of the question; namely, the conditions obtaining in a sexually mature female when no extracts are injected. Earlier in the paper it has been shown that, although the pituitary was removed shortly after mating, ovulation was followed by a normal growth of the corpus luteum for a two day period. It is evident that, if the granulosa is acted on by two hormones, one causing growth of the granulosa, the other luteinization, the two must be present in these animals at the same time. There must be a "selective utilization" of these hormones by the granulosa before and after follicular rupture. The follicular growth followed by ovulation and the lutein transformation cannot under these conditions be due to the successive secretion by the pituitary of a follicle or gonad-stimulating hormone and of a luteinizing hormone.

In the intact animal a similar condition exists, at least in some forms. In the pregnant rabbit the follicles grow and reach the size that is attained in the non-pregnant estrus animal. These animals will mate. Ovulation is induced by the injection of the urine of pregnancy.[9] The confirmation of this and even ovulation after injection of a saline suspension of anterior hypophysis has been recently reported by Wolfe.[10] In the rat during gestation, mating [11] may occur. Even the cyclic formation of normal follicles followed by luteinization [12] has been reported. If there are two pituitary sex hormones, it is evident that in these cases both are present throughout pregnancy and that here as well as in rabbits hypophysectomized shortly after mating there must be a selective utilization of them by the ovarian elements. Follicular growth and luteinization under physiologic conditions thus cannot be explained by the successive secretion by the pituitary of two hormones. The luteinizing hormone, if it is a specific hormone, is present throughout, for the corpora lutea of pregnancy are being maintained. In its presence, follicular growth and maturation take place. Factors such as toxicity of extracts or nonphysiologic rates of growth of the granulosa, leading to its premature entrance on the second phase of its cycle, namely, luteinization, may be responsible for the luteinization effects of extracts, rather than the fact that they contain a specific luteinizing hormone.

6. Engle, E. T.: Ovarian Responses: Differences Elicited by Treatment with Urine From Pregnant Women and by Freshly Implanted Anterior Lobe, J. A. M. A. **93**: 276-277 (July 27) 1929.
7. Fevold, H. L.; Hisaw, F. L., and Leonard, S. L.: The Gonad Stimulating and the Luteinizing Hormones of the Anterior Lobe of the Hypophysis, Am. J. Physiol. **97**: 291-302 (May) 1931.
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9. Hill, M., and Parkes, A. S.: The Action of the Ovulation-Producing Substance of Urine of Pregnancy on the Hypophysectomized Rabbit, J. Physiol. **71**: 40-46 (Jan.) 1931.
10. Wolfe, J. M.: Ovulation in the Pregnant Rabbit, Anat. Rec. (preliminary abstract), 1931.
11. Nelson, W. O.: Estrus During Pregnancy, Science **70**: 453 (Nov. 8) 1929. Long, J. A., and Evans, H. M.: The Estrous Cycle in the Rat and Its Associated Phenomena, Memoirs, University of Calif. **6**, 1922.
12. Swezy, Olive; and Evans, H. M.: Ovarian Changes During Pregnancy in the Rat, Science **73**: 46 (Jan. 10) 1930.

SUMMARY

Rabbits have been hypophysectomized by a procedure that permits prolonged survival.

Ovulation will take place although the pituitary is removed after a postmating period but slightly over an hour in length, thus confirming the report of Fee and Parkes. In such animals the corpora lutea develop normally for approximately a two day period. Further changes are atypical.

The development of the corpora in the absence of any postovulatory pituitary secretion is discussed in regard to its bearing on the question of the unity or the duality of the pituitary sex hormones.

THE PHYLOGENY OF MENSTRUATION*

CARL G. HARTMAN, PH.D.
BALTIMORE

A little over a hundred years ago the medical world experienced a flurry when the French anatomist Cuvier announced that menstruation could no longer be considered a distinctly human characteristic, since he had found (as had indeed a few forgotten authors before him) that female apes and monkeys share with women this periodic bleeding phenomenon. The menstrual process was therefore set down as a primate character, particularly since, as Heape first pointed out, the menstrual cycle in both monkeys and women involves identical changes of the reproductive organs.

The general biologist may concede that in its spectacular manifestations menstruation is a "primate character." But if one searches for fundamental or even for the more superficial physiologic causes, and if one investigates other mammals and even the lower vertebrates and attempts to discover what they have in common with man, anthropocentric ideas receive jolt after jolt. I propose to show the universality of uterine bleeding in the vertebrate series and to offer this generalization as another example of the kinship of man with the whole of creation. Perhaps, eventually, the traditional attitude of the medical man who considers the human body as something apart from brute creation will eventually disappear entirely, leading to a better understanding of the body which it is attempted to improve or cure. There is nothing essential or physiologically important about the human body that is not already present or clearly foreshadowed in the lower forms. To illustrate this by examples nearer to my theme, fact on fact is accumulating to demonstrate the generalized character of the reproductive process, and I propose to show that uterine bleeding is no exception.

* From the Carnegie Laboratory of Embryology, Johns Hopkins Medical School.
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Sixty years ago it was still held that menstruation constitutes a preparation for the reception of the egg, which, it was held, was discharged at or about the menstrual period. The entire theory of menstruation started with this assumption. After much painstaking labor on the part of the gynecologist it is now known that ovulation occurs almost exactly in the middle of the cycle. On this fact there was immediately elaborated another far-reaching theory of menstruation which emphasizes the ovarian factor, the corpus luteum, or rather its degeneration, as the cause of menstruation, a *post hoc, propter hoc* theory which in its turn is quite devoid of any experimental proof. The theory is still in vogue, however, despite the fact that the work of Heape, van Herwerden, Corner and Allen has shown that the corpus luteum is unessential to the menstrual rhythm. A large mass of material from the Carnegie monkey colony, shortly to be published, involving hundreds of menstrual cycles, precisely diagnosed as to whether ovulatory or nonovulatory, should finally convince the student of the problem that an extra-ovarian factor is involved in the menstrual flow. Clinically the uterine bleeding is undifferentiable whether it occurs from a 12 mm. hard, interval type of uterus, accompanied by a "resting" ovary, or from a 22 mm. soft, succulent, vascular organ produced under the stimulus of a corpus luteum.

The challenge to point out the extra-ovarian factor concerned in bleeding was met by the Carnegie Laboratory through a cooperative piece of work (Hartman, Firor and Geiling), in which the possible rôle of the anterior pituitary was analyzed. It was found that uterine bleeding which the ovarian hormone produced when injected into monkeys (Allen) was ineffective when injected into the hypophysectomized animal, whereas in such, as in normal animals, anterior lobe substance in any form always caused bleeding. These experiments mark a beginning in the analysis of the process.

But the problem is not a simple one. To the biologist it has broad ramifications. He thinks of menstruation as just one more form of uterine bleeding which begins, as shall be shown, with the cartilaginous fishes and therefore goes back far into geological time. Perhaps the essential physiology of menstruation has a more venerable history than has been imagined.

In the monkey there are many types of uterine bleeding. Aside from the postpartum hemorrhage, the bleeding presaging abortion, and different types of pathologic bleeding, there are as regular or frequent occurrence: (1) menstruation with ovulation; (2) menstruation without ovulation; (3) the placental sign or bleeding of implantation, and (4) the intermenstrual or mittelschmerz bleeding. Leaving out the last as the more obscure (the probable homologue of the estrous bleeding of dogs and cows), I am tentatively considering menstruation and the placental bleeding as homologous; that is, conditioned by the same physiologic factors. The close connection between menstruation and reproduction, on which three profound students of the problem, Robert Meyer, Robert Schröder and Emil Novak, have insisted, thus attains a new significance. The fact is that throughout the vertebrate series, wherever the embryo lives in a brood chamber at the expense of the parent beyond the point to which the stored yolk of the egg carries it, there one finds bleeding into the brood chamber. This is true of man and of monkey, the "menstruating" forms that have a particularly hemorrhagic type of implantation; it is true of other forms having a burrowing type of placentation, such as lemurs, carnivores and rodents; and it is equally true of the nondeciduates, like the sheep and the cow. In many of these the bleeding into the uterine cavity has been described and the erythrocyte content of the "uterine milk" studied (Bonnet, Kolster). Because of the widespread nature of the phenomenon, its students have ascribed to the hemoglobin and its derivatives a nutritive function, probably most often a means of conveying iron, perhaps at times conveyance of oxygen itself.

Passing to the predominantly egg laying classes of vertebrates (fishes, amphibia, reptiles, birds) one finds that, in all except the birds here and there, in species, genera or even whole families, life habits have become associated with viviparity, intra-uterine or intra-ovarian development, even to the extent of yolk sac or allantoic implantation. Here one encounters the same story over and over again: where the embryo depends for development beyond the egg stage on the mother's (or the father's) body substance, there one may find in the brood chamber red blood cells mingled with the pabulum provided by the nutritional organ.

With the exception of certain brood pouches as the back of the Surinam toad, the gular pouch of Darwin's toad, the pouch of the male sea-horse and pipe-fish, the nutritive organs are the derivatives of the müllerian duct. This is practically the only mucous membrane in the body through which the passage of red blood cells is a physiologic process. Is this under the control of the anterior lobe? If so, this gland already shows a difference of function in the pregnant and in the nonpregnant shark. This principle is susceptible of test by experiment on the appropriate species.

From among the great variety of conditions under which the embryonic nutrition is effected in the various truly viviparous fishes and amphibia, let us select three:

1. Many eggs of *Salamandra atra* are shed into the oviduct, but only one or at most two embryos are destined to develop and to be born; the survivor lives at the expense of the abortive eggs, swallowing them bodily as it floats in the embryotrophic "soup" provided by the oviduct. This semifluid mass is laden with red blood cells, according to Wiederscheim to provide oxygen directly to the embryo.

2. In the stingray *Pteroplatea* there grow out from the uterine wall long slender threads (trophonemata) which are highly vascular and covered with secreting glands. These strands enter the gill-slits of the embryo, hang into the gut and become not stomach tubes but secretory stomach villi. Their secretion feeds the embryos. Red blood cells find their way into the uterine cavity and the embryonic intestines.

3. *Zoarces*, a bony fish, has an intra-ovarian method of reproduction in which the spent follicles or corpora lutea literally and directly feed the developing embryo. The phenomenon is a kind of diagrammatic representation of the so-called trophic function of the corpus luteum of pregnancy, postulated by some writers on the corpus luteum. The shed eggs of *Zoarces* remain within the ovary, held in place by the emptied follicles, which metamorphose into corpora lutea in the form of secretory villi. They become greatly injected by capillaries, which form veritable retia mirabilia. Secretion increases according to the needs of the growing embryos, which remain within the ovarian chamber until birth. In the embryotrophic substance of the ovarian chamber and in the gut of the embryo, red and white blood cells are found in numbers. Stuhlmann thinks

that the blood serves the purpose of oxygenation directly. How blood gets into the ovarian cavity this author is at a loss to say, since he finds the blood vessels intact. With his failure to analyze the mechanism of bleeding in *Zoarces*, I have a sympathy, as the same difficulty is encountered in explaining the blood loss of the bitch and the cow at heat and the monkey during the intermenstrual bleeding.

Sufficient has been said to introduce those who have not thought of the matter to the widespread occurrence of bleeding into the müllerian derivatives. The study of the control of the bleeding has not yet begun, so far as the lower vertebrates is concerned. The suggestion of Hartman, Firor and Geiling that a hypophyseal factor may be generally involved seems to me to be worth following up. The common denominator in the physiologic control of the various types of bleeding is likely to be the fundamental principle involved. Menstruation according to this view begins with the Salachian fishes—and there is again "nothing new under the sun."

Wolfe and Madison streets.

ABSTRACT OF DISCUSSION

ON PAPERS OF DR. FRANK, DRS. G. V. S. AND O. W. SMITH, DRS. BURCH, WILLIAMS, WOLFE AND CUNNINGHAM, DR. SMITH AND MR. WHITE, AND DR. HARTMAN

DR. EDGAR ALLEN, Columbia, Mo.: Dr. Frank finds that the amount of theelin in the blood and that excreted in the urine increase before menstruation. In quantitative analyses of the theelin content of human ovarian tissues, Drs. Pratt and Newell and I found greater amounts of theelin at the time of ovulation; i. e., in the interval of the menstrual cycle. Perhaps the suggestion made by Drs. G. V. S. and O. W. Smith that there is a change in the threshold of excretion will be the answer to these differences. The matter of a name for follicular hormone is urgent. Five different names are now in use: "follicular hormone," "estrin," "amniotin," "female sex hormone" and "theelin." Dr. Doisy's name for the crystalline material which he has isolated is "theelin." I propose its more general use. The paper by Dr. Smith and Mr. White presents one of the outstanding achievements of recent years. I have noted in the clinical literature that Zondek and Aschheim have obtained priority in some citations for this work. Dr. Smith has concerned himself little with discussion of priority. Careful scrutiny of the literature will determine that publication by Smith and Engle preceded that of Zondek and Aschheim. I was greatly interested in the discussion of mitosis by Drs. Burch, Williams, Wolfe and Cunningham. The action of theelin is principally to cause division of cells of the accessory genital tissues. Their suggestion that progestin may in some way stop growth of the tissues after ovulation is interesting. I wish that Dr. Hartman might have talked further about the matter of anterior hypophysis stimulation of menstruation. With the anterior lobe intact in castrated animals, enough growth can be induced in the endometrium by injections of theelin so that, when injections are discontinued, menstruation begins. To just what extent the anterior lobe can work independently of the ovary should be studied further. Dr. Hartman's negative results in a castrate of eight months might give an indication, at least, that some growth in the endometrium from the action of theelin is required before menstruation can be produced.

DR. FREDERICK L. HISAW, Madison, Wis.: I propose to limit my remarks to the physiology of the corpus luteum. At present it is known that the corpus luteum of the sow secretes not one hormone but three, in addition to estrin. Progestin, then, or corporin, as we speak of it in our laboratory, is only one of the three. Corporin acts on the uterus and perhaps produces other physiologic changes. Another hormone, relaxin, acts on the pelvic ligaments; it does nothing else, so far as is known. A third hormone acts on the vaginal mucosa of rodents, producing mucigenation typical of the condition found during pregnancy. I wish to speak about the action of corporin on the endometrium. Dr. Allen has shown that theelin stimulates endometrial growth in monkeys, and its discontinuance is followed by menstruation. We have found that theelin at a given dosage (40 rat units daily) can be continued presumably indefinitely (forty days at least) without signs of menstruation, but if this dosage is lowered (20 rat units daily), menstruation occurs. A decrease of the dosage, then, or a discontinuance of theelin treatment is followed by menstruation. The endometrium is characterized by numerous mitoses, low glandular mucosa (from 35 to 40 microns), only slight coiling of the glands, and, at the time of menstruation, no premenstrual swelling of the gland cells and little or no fraying of the mucosa. When these conditions are produced in a castrated monkey, and the theelin treatment is replaced by injections of corporin, a typical premenstrual condition is developed. The uterine glands are coiled and dilated, the glandular mucosa is high (from 70 to 80 microns), mitoses are very few or absent, and just previous to menstruation there is a pronounced fraying of the mucosa. Corporin, then, modifies the theelin type of endometrium into the premenstrual type normally associated with a corpus luteum. When theelin in large doses is given simultaneously with corporin, only the theelin effects are seen; that is, theelin overrides corporin. This reaction, then, is one in which theelin must act first, followed by corporin, as corporin cannot modify the uterus of an untreated castrate. Neither does corporin seem to postpone the time of bleeding following discontinuance of theelin treatment or postoperative bleeding following ovariectomy.

DR. CARL R. MOORE, Chicago: This symposium has been intensely interesting, to a certain extent enlightening, and also to an extent confusing, because of the various aspects presented and the differences occurring among animals of different species. I have sympathy for the clinician who is presented with problems of hormonal administration, for even in the laboratory, with experimental animals, it is often difficult to bring a creditable interpretation to bear on repeatable results. The phase of these problems of most interest to me is the demonstrable links between the different gland activities and their influence on one another. In my experimental work I have recently offered certain suggestions regarding the nature of these interlinkings, and the present discussions have contributed materially to this conception. The chief aspect that the clinician should bear in mind is that the administration of sex hormones (theelin, estrin, testis hormone and the like) so acts on the anterior lobe of the hypophysis as to diminish the gonad-stimulating hormones available and, as a result, injury to the gonads occurs. Perhaps the clinician has often attempted a stimulation of a so-called hypogonadal state, ephemeral as this may be, by administration of preparations of the female or the male hormone. In actual laboratory observations, however, instead of a stimulation there is really an injury to the intact gonads. Substances produced by the ovary do not stimulate its activity, nor do substances produced by the testis stimulate this organ. The injury produced on both appears to be due to the hypophyseal depression from the gonad hormones. This reciprocal relation has been indicated in many of the papers presented today and by the remarks of other speakers. How many other endocrine glands will prove to have a place in the chain of events is impossible to predict at present. The report of Drs. Burch, Williams, Wolfe and Cunningham, in which it is shown that the activity of the hypophysis varies with the amount of the female hormone present, substantiates the reciprocal nature of the interactions between the hypophysis and the ovary.

DR. JEAN PAUL PRATT, Detroit: This symposium suggests to the clinician many possibilities for diagnosis and treatment, but a word of caution is necessary, not to draw conclusions too hastily from the results of animal experiments. Estrus of animals must not be confused with menstruation, for the conditions are not identical. Disturbance of menstruation is one of the best indicators of abnormality of sexual organs and therefore it is natural that one should look for some regulator of menstruation. Even the fact that monkeys menstruate must not lead one to conclude that their menstruation

is similar to human menstruation, or that the two primates will necessarily respond in a similar way to glandular products. In 1926, in this section at the Dallas meeting, I reported the injection of the follicular hormone in women and noted at that time that one could get definite evidence of growth of the uterus. I had hoped to be able also to report bleeding, but in many attempts there has been no evidence of menstruation being reproduced by the injection of theelin; in many observations, however, the evidence of growth has been repeated. So far as I can see clinically, the only thing that one can expect to get from theelin is growth of the uterus. There have appeared in the literature reports ascribing beneficial results from the use of theelin in dysmenorrhea and in combating symptoms of the menopause. In my experience this conclusion is not justified, for equally good results may be obtained by injection of sterile water, or by other psychotherapeutic measures. For, after all, the symptoms of most dysmenorrheas and the menopause are largely psychic. The suggestions in the symposium give great hope for future therapy, but a great deal of work is necessary to translate the results of animal experiments into terms of human therapy.

DR. M. A. GOLDBERGER, New York: Our interest has been mainly in studying the occurrence of the female sex hormone, as we call it and the anterior pituitary hormone, in the human female. The first chart that Dr. Frank showed might be emphasized; in this the method of extraction of the female sex hormone was graphically produced. Whereas previously we used to throw the blood sludge away after the female sex hormone was extracted, we are now able to use that sludge and extract the anterior pituitary hormone.

DR. CHARLES MAZER, Philadelphia: The degree of uterine development should be the main guide in the administration of female sex hormone or estrin. The product does not exert any action on the ovaries. It does, however, produce growth and vascularity of the uterus. If the uterus is normal in size, the existing condition is usually due to failure of the second phase of the ovarian cycle, luteinization, for which the luteinizing hormone of the anterior lobe of the pituitary gland should be administered. In my experience, low voltage irradiation of the ovaries and pituitary gland is the most effective agent in restoring menstrual periodicity. The functional menorrhagias and metrorrhagias likewise respond to this treatment.

DR. ROBERT T. FRANK, New York: I pity the clinician—and I am one—if he attempts to translate into clinical medicine what the advance guard is feeling out in physiology. We have had a great disappointment in that theelin (I think that it is time to adopt one name and, in deference to Dr. Doisy's epoch-making discovery of crystallization of this product, I think we might use that name) works harmfully on the ovary. I cannot see how it can act in a stimulating fashion, and I predict that we shall meet with similar disappointments when we have a commercially active product to use on the human being. Dr. Smith and Mr. White brought out that the amount of a hormone that one finds in a gland is no indication whatever of the amount that it is secreting into the circulation. Dr. Allen mentioned or referred to a change in threshold of the kidney toward the excretion of theelin. The work in our laboratory has definitely shown such a change in threshold, as we reported last year in several papers. Whether any other explanation can be found is yet to be seen. The time has also arrived to call a halt in ascribing every part action of a hormone to a special hormone. For instance, to have collected eleven factors for the prepituitary is carrying the thing to an extreme. Further study will probably show that simplification is possible. Our old concept, at least our old histologic concept, of menstruation should be kept up for the time being until we have a more definite conception of what the exact mechanism of the menstrual bleeding is. Finally, I want to call attention to a clinical application. The physician who would not think of treating a patient with thyroid extract in a thyroid disturbance or in any disturbance of metabolism, without making a basal metabolism determination, the physician who insists on taking frequent samples of blood to note the sugar level in a case of diabetes or suspected diabetes, or the physician who insists on electrocardiograms in every case of organic and functional heart disease still seems to balk and hesitate in applying these blood and urine hormone tests, which are available and which are comparatively simple, in clinical and in functional disturbances of the genital system, otherwise entirely indistinguishable and readily confused with one another.

DR. PHILIP EDWARD SMITH, New York: I want to say a word about the proposal of Dr. Allen that the female sex hormone or follicular hormone be called "theelin." This is a patented product and it appears to me improper to use in our scientific papers a patented name to designate an active principle. The matter of patents affects the investigator, the practitioner and the public. There is at present a general and unfortunate tendency to patent all products discovered in the laboratory. The assurance that pharmaceutic houses will place on the market properly standardized products is important, but is it getting at the problem in the proper way for the investigator to patent his discoveries? I am not referring particularly to theelin, which is the least objectionable of the examples. Should the investigator or the laboratory or the university levy tribute from the public for these discoveries? There is enough wealth in this country to support investigation, and this wealth will be more freely given if there are not any royalties. I think that the American Medical Association could well sponsor the setting up of a national body for the standardization of these products. The investigator would then have no reason for patenting his discoveries and the element of commercialism need then not enter into his research work. In connection with Dr. Frank's paper, I believe that the assays which he is making of the content in the blood of the anterior pituitary hormone are giving invaluable information. It is the hormone that is secreted into the blood that counts; it is not the hormone that is stored in the gland. The assay of pituitary activity by implants gives an indication of the stored hormone of that gland; it may not give any information in regard to the amount of the hormone being supplied to the animal. Implants of the thyroid, for instance, would give an entirely erroneous picture of the amount of secretion which goes into the circulation in exophthalmic goiter and in colloid goiter. It is by using the blood assay method in which Dr. Frank is pioneering that we shall get information of the greatest value.

DR. JOHN C. BURCH, Nashville, Tenn.: One of the most interesting phases of this work is the different action of the various hormones in varying concentrations. This is well shown by Friedman's work on the rabbit. It is important to remember that the amount of hormone circulating in the blood and at the point of action is the essential thing. In regard to the apparent contradiction between the work of Dr. Hisaw and his co-workers and that of Dr. Cunningham and myself, I wish to state that our donor rats were injected with large amounts of an alcoholic extract of human placenta over a short period of time. Following this method we got an increase of the ovarian-stimulating power of the anterior hypophysis. Dr. Hisaw found that when estrin was injected over a long period of time the reverse was true and there was no stimulation. It is possible, therefore, that these two sets of experiments were different in the type of substance injected (because placental extracts may contain some factor other than estrin) as well as in the duration of the injections. Variations in either of these two factors may have been responsible for the difference in the results.

DR. GEORGE VAN S. SMITH, Brookline, Mass.: The term "luteinizing hormone" for the substance prepared from the urine of pregnant women may be incorrect, for, when given intravenously, it produces ovulation as well as luteinization. The recent work of Evans indicates that this hormone is active on the ovaries only if the anterior hypophysis is present. Hence the ovarian effects may be due entirely to its stimulation of the anterior hypophysis. I was glad to hear Dr. Hisaw bring up the subject of quantitative endocrine relationships; e. g., small amounts of theelin are necessary for the progestational proliferation of the endometrium caused by progestin, but large amounts inhibit the action of progestin. This situation seems to be true also in the matter of lactation. Some of the experimental discrepancies may be found due to incorrect dosage. Dr. Ernst Philipp of Berlin implanted portions of the anterior lobes of the pituitary glands of three patients who died shortly after delivery and found the ovaries of the test animals unaf-

fected. This observation indicates again that the sex hormones of the anterior hypophysis are depressed after the middle of pregnancy and during lactation, as gaged by the regression of the corpus luteum and the absence of ovulation. I feel that enlightenment in these matters will depend on the studies of lactation that are now being pursued.

DR. CARL G. HARTMAN, Baltimore: I wish to thank Dr. Novak for giving others the chance to criticize my views, and I will take to heart Dr. Frank's suggestion as to the name, although I must say that names will not get one anywhere in studying physiologic causes. I am sorry that Dr. Hisaw did not discuss further the relaxing hormone, because Dr. W. L. Straus, one of my colleagues, has found that in the monkey there is a definite relaxation of the symphysis, so much so that one can put one's finger into the slit formed by spreading the ischial tuberosities. This takes place within the last three weeks of gestation, and the ligaments are again thoroughly knit up within ten days after parturition. No matter how hard one pulls, one can't get a spread of over 3 mm. in the normal animal, whereas it is easy to get a spread of 15 mm. with rather moderate pressure at which the puerperal monkey flinches with pain. Lastly, one other warning as to the gaging of results: Dr. Friedman has obtained most variable results with the study of his method of causing ovulation not only by the route of administration, namely, whether intravenous, intraperitoneal or subcutaneous, but also by the distribution of the dosage over a period of time.

SLIPPING OF THE UPPER FEMORAL EPIPHYSIS

A STUDY OF SEVENTY CASES *

ALBERT B. FERGUSON, M.D.
AND
M. BECKETT HOWORTH, M.D.
Fellow of New York Orthopaedic Dispensary and Hospital
NEW YORK

A condition occurring between the ages of 8 and 17 years is described in the literature as epiphyseal fracture, separation, or slipping, epiphyseal coxa vara, adolescent rickets, pathologic fracture, and femoral osteochondritis of adolescence. It is a disease characterized by weakening of the epiphyseal disk at the femoral head, permitting subsequent displacement of the head on the neck.

We are presenting a study of seventy cases of this disease from the New York Orthopaedic Dispensary and Hospital. Sixty-three were seen in adolescence; seven were adult residuals. Thirty-nine were in males, thirty-one in females. In thirty-one cases only the left hip was affected; in twenty-four the right, and fifteen were bilateral. Bilateralism is about as common as in coxa plana and only slightly more common than in frank infections.

Of fifty-five patients, 65 per cent were overweight, half of them having endocrine imbalance. Many of the overgrown children were of the type described by Mikulicz—a large child with flabby, weak musculature and more than the usual subcutaneous fat. Often a patient, obese in adolescence, was normal or even slender five or ten years later. In four cases endocrine therapy was tried with no effect on the epiphyseal disk, although weight was reduced. Many grew rapidly in height or weight just before the onset. A number of slender patients were tall for their age, thus having more than the usual weight on their hips.

Premature union of growth centers, as compared with the normal side, is usual at the affected hip in the trochanters, head and acetabulum. It was noted at 12 years in one girl. The same thing may be noted in other inflammations at the hip. It is therefore considered as evidence of the wide extent of circulatory disturbance in the region. It does not indicate endocrine imbalance, as it is not seen in the unaffected hip or in other regions of the body.

At or shortly before the onset, twenty-four patients out of forty-five (53 per cent) had tonsils diseased or removed, five (11 per cent) had appendicitis, and five had other infections. Seventy-five per cent had some definite infection, which suggests that infection elsewhere may be an etiologic factor.

THE RÔLE OF TRAUMA

Trauma hastens the onset of symptoms and initiates or increases displacement. The trauma is usually trivial and rarely more than occurs in the normal activity of the average child. Greater displacements are more common with trauma which might have been severe. Displacement may be gradual with no trauma. One case showed displacement of two-eighths, three-eighths, four-eighths and five-eighths inch at successive examinations with no injuries and with no aggravation of symptoms. Trauma may aggravate the displacement at any time. We have found no differentiation into traumatic and nontraumatic types.

CHARACTERISTICS OF ONSET

The age at onset in thirty-six boys was from 9 to 16 years with 75 per cent between the twelfth and fifteenth birthdays. In the cases beginning before the age of 12 years there was unusual stress on the epiphyseal line by reason of severe trauma or excessive overweight. Uninfluenced by these factors, the age at onset was from 12 to 16 years for boys.

Symptoms were present before displacement in seventeen hips in thirteen boys. Those younger than 13 reached that age before slipping occurred, the preslipping stage averaging thirteen months. Preslipping stages beginning after 13 averaged only five months. Prompt displacement is apt to occur at the age when epiphyseal cartilage is forming bone rapidly.

Displacement occurred in thirty-three of the adolescent boys; 66 per cent slipped between the thirteenth and fifteenth birthdays. This is the age of slipping for boys. The six younger boys (aged from 9 to 12 years) were subject to unusual stress in the form of severe trauma or excessive overweight. Unusual stress may be regarded as the cause of displacement before the slipping age period. Conversely, the five boys whose first displacement occurred after the fifteenth birthday were not materially overweight or remembered no trauma up to the day of slipping.

In the five months from July to November, 66 per cent of the boys had onset of the disease and 70 per cent had onset of the displacement. This incidence expresses the seasonal activity of the boy—the period of vacation and of football playing.

Analysis of the years of onset showed no epidemic features.

The age of onset of symptoms in girls was from 8 to 13 years, with 89 per cent occurring between the tenth and fourteenth birthdays. Displacement occurred at the tenth to fourteenth year, with 87 per cent between the eleventh and fourteenth birthdays. The seasonal incidence was one month earlier for girls; their period of activity was not prolonged by football. The girls

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outside the usual age period and the female preslipping cases showed the same relations to trauma, excess weight and duration of the preslipping stage as have been noted for boys.

PATHOLOGY

Twelve hips have been opened at operation. In the specimens examined, the bone and epiphyseal line showed no evidence of rickets, infection or osteomalacia. The capsule and periosteum about the neck were thickened, sclerosed and avascular. These changes were present in the hip operated on in the preslipping stage (fig. 1).

CLINICAL FEATURES

There are four stages of the disease—preslipping, slipping, quiescent and residual. When there are no acute signs and no spasm, the lesion is quiescent. When the lesion is quiescent and the epiphyseal line is united, it is residual.

In these cases we have found the following: In the preslipping stage limp and pain are usual; fatigue, stiffness and disability are frequent (table 1). Examination reveals limp, pain on motion, and often spasm or atrophy. All motions except extension tend to be limited, internal rotation being most commonly affected. When the hip is flexed it tends to abduct and rotate externally, allowing further flexion. After slipping has occurred, the symptoms and signs are more pronounced. Complete disability is often present but is not dependent on the amount of displacement. Shortening, tenderness and, occasionally, crepitus and swelling may appear. When the femur is rotated, the head may be palpable under the gluteal muscles—a sign almost pathognomonic of slipped epiphysis. In

TABLE 1.—*Clinical Features*

	Before Slipping, Per Cent	After Slipping, Per Cent
Symptoms:		
Limp	93	96
Pain	100	93
Fatigue	83	78
Stiffness	90	94
Disability in athletics	67	93
Physical Signs:		
Limp	88	84
Pain on motion	71	92
Spasm	67	84
Tenderness	33	98
Shortening	17	85
Atrophy	45	71
Limitation of Motion:		
Flexion	67	84
Abduction	64	92
Adduction	44	84
Internal rotation	86	98
External rotation	77	85
All motions	..	71
Deformity:		
Flexion	0	*
External rotation	11	67
Adduction	..	27

* As the absence of flexion deformity was not apt to be recorded, its incidence is indefinite. Flexion deformity, when present, was slight.

the quiescent stage, the signs and symptoms have subsided and may be less than in the preslipping stage; spasm has disappeared. Limp, pain, fatigue and limitation of motion often persist into the residual stage.

ROENTGENOGRAPHIC OBSERVATIONS

In the preslipping stage the epiphyseal line is abnormally wide; the end of the neck may be irregular and somewhat decalcified. Thickening of the capsule may be recognizable at the margins of the joint. Most of the other epiphyseal lines in the region are somewhat closer to union than on the normal side.

In the slipping stage the same changes are present, and there is a varying degree of upward displacement, external rotation and adduction of the neck on the head. The displacement of the head uncovers the end of the neck superiorly and anteriorly. Callus may be present in the angle between the head and neck inferiorly; as it matures it may obscure the original

TABLE 2.—*Example of Index of Motion*

	Motion	Factor	Product
Flexion	145	0.4	58
Abduction	45	0.4	18
Adduction	30	0.2	6
Internal rotation	30	0.2	6
External rotation	60	0.1	6
Extension	10	0.1	1
Index of function			95

Hypermobile	over 110
Normal	90 to 110
Good	60 to 90
Fair	50 to 60
Indifferent	40 to 50
Poor	30 to 40
Bad	under 30

outline of the neck and give the appearance of an epiphyseal line in a plane more vertical than usual. Examination with the femur rotated internally causes the shadows of the head and neck to superimpose, simulating reduction of displacement.

After quiescence, the callus is mature, there is no decalcification unless there has been confinement in plaster, the end of the neck is less irregular, and the epiphyseal line is narrow.

In the residual stage, ossification of the epiphyseal line is completed and slight calcareous deposits indicating arthritis may appear at the articular margins. Arthritic changes are more extensive and more definite several years later.

Marked lumbosacral anomalies, such as a transitional type of vertebra, were present in 43 per cent of the cases.

DIAGNOSIS

A child between 8 and 18 years of age complaining of a limp, or pain in the hip, thigh or knee may have a preslipping or slipped upper femoral epiphysis. The hip should be carefully examined for limitation of motion, particularly internal rotation and abduction, and for spasm at the limits of motion. The presence of these physical conditions necessitates roentgenographic examination, by which the diagnosis can almost always be established. Questionable cases should have careful observation, limitation of activities, and repeated roentgenographic examinations.

The roentgenographic and other features of this condition are so different from those of other conditions occurring in this age period, such as tuberculosis, fracture, dislocation, residuals of coxa plana, osteomyelitis and suppurative arthritis, that discussion of differential features is superfluous. The active stage of coxa plana is usually confined to children under 10 years of age. The absence of changes in the epiphyseal line distinguishes nonsuppurative arthritis.

METHODS OF EVALUATION OF RESULTS

If operative procedure does not correct displacement, the operation has failed. Since upward displacement of the neck is the most important deformity to correct, is the easiest to measure, and is usually corrected when

anything is accomplished, this may be used for convenience as the measure of the success of the operative procedure. Judging displacement requires great care. Rotation and callus formation obscure the relation of the head to the neck. To check the interpretation, additional measurements may be used—the distance from the head to the lesser trochanter, the adduction of the neck relative to the axis of the head, the amount of the end of the neck uncovered by the head superiorly.

The function of the hip may be expressed by means of an index. If each motion of the hip is arbitrarily evaluated for its importance in function, the index will be obtained by multiplying the degrees of each motion by the constant of value and adding these sums. The constants we have used are:

For flexion and for abduction..... 0.4.
For adduction and for internal rotation... 0.2.
For external rotation and for extension 0.1 (table 2).

We shall use this index to express the functional result in these hips. As improvement in symptoms accompanies improvement in function, the index offers a fair statement of the outcome of the case. A normal hip has an index of between 90 and 110.

RESULTS

In judging the results of operative procedures, comparisons must be made with the results in cases in which operation was not performed. Fifteen hips were given no operative treatment. Their displacement varied from zero to five-eighths inch; in four it was three-eighths inch or more. Twelve had treatment by bed or caliper brace; three had no treatment. All with good function improved; all with impaired function improved greatly; in all, the symptoms were much improved or eradicated. This record was not approached by most operative procedures that we have used.

There are thirty cases that were followed to the residual stage. At the last examination the ages of the patients varied from 12 to 27, with an average of 17 years. The time since the last orthopedic treatment varied from five months to fourteen years, with an average of three and a half years and a mean of three years. The age at operation had no detectable influence on the result, although with closed reduction in a young patient it is possible that further slipping might occur.

Fig. 1.—Sclerosis and avascularity of the tissues about the femoral neck. The specimen is from a patient operated on in the preslipping stage.

CLOSED REDUCTIONS

Closed reductions were usually forceful abductions followed by forced internal rotation. In twenty-one cases, closed reductions of this type were utilized. Eighteen closed reductions failed, six patients having subsequent open operations. Two were about 50 per cent successful; one was almost completely successful but displacement was slight in these three. Operations were performed within one month of the onset of symptoms and within three and a half weeks after displacement.

The functional results following abduction manipulation are judged in the eighteen cases which we have seen in the residual stage. Two of these had partial correction; one was improved from an index of 20 and displacement of 1⅛ inches to a final index of 96 with displacement of five-eighths inch; another was improved from an index of 12, displacement of seven-eighths to an index of 34, displacement of five-eighths. Of the remaining sixteen patients, all unimproved anatomically,

Fig. 2.—Result of manipulation in hips with similar displacements. On the left the abduction method was used unsuccessfully. The right was reduced by traction four weeks after slipping. Callus projects inferiorly at the end of the neck on the right.

twelve had a final index of below 50; four had hips which were good functionally, but one was worse than before manipulation. All but one of the unsuccessful attempts at reduction were performed more than four months after the onset of symptoms and more than one month after slipping, and callus was present in each case. The three displaced hips having no attempt at reduction show results as good as manipulated hips with similar displacements.

We have tried reduction by traction in seven cases this year, with some success anatomically (fig. 2), but we have as yet only limited knowledge of the functional result. Manual traction of from 300 to 600 pounds is gradually applied with the aid of stirrups at the ankle and knee, the leg being adducted. When it is believed that reduction has occurred, the leg is rotated internally, force being used if necessary. It is then roentgenographed and, if reduced, a double spica is applied in abduction and internal rotation.

Traction was also used in 1922 in two cases. Each was successful anatomically. Each operation was done five days after slipping and within two months of the onset of symptoms. The indexes of function in the residual stage were 70 and 100. They were symptomless except that one patient had some pain in wet weather or when fatigued.

OPEN OPERATIONS

Open reductions were attempted in eleven cases, with fair anatomic success in three. The Smith-Petersen approach was used. Five of the eleven hips had the head freed at the epiphyseal line; six had cuneiform osteotomy near the line. Visible epiphyseal cartilage was removed and the displacement corrected. The leg was immobilized, usually in abduction, internal rotation

and extension. Seven of these—five of which had attempts at closed reduction—were followed to the quiescent or residual stage. Only three showed any notable improvement anatomically; these were improved functionally but still had low indexes, 51, 47 and 33. Of the four that were not materially improved anatomically, one was functionally slightly better, one was slightly

Fig. 1.—Marked bilateral displacement with good function. On the left the index of function was 73; on the right it was 83. There was no operation.

worse, and two were much worse. These results do not compare favorably with cases in which no attempt at reduction was made. Probably a bar to successful reduction in these operations was callus formation on the neck inferiorly which would catch in the margin of the head. This suggests the need of exposing this area at operation so that the callus can be removed and the head pushed up. All these open operations were in cases of long standing, with marked callus formation. It is quite possible that open operations done in fresh cases might show much better results.

Subtrochanteric osteotomy was done in four cases with displacement from five-eighths to seven-eighths inch. One was a stiff hip in adduction deformity which was relieved. The others showed flexion or extension of the upper fragment after operation. In one case this added 2 inches (5 cm.) to the shortening. This case was not improved functionally. The remaining two cases were materially improved and attained indexes of 80 and 70.

Two patients eventually had reconstruction operations, one after four attempts at reduction, including an open operation; the other after an attempt to hold the head in place with a spike which penetrated the joint.

RELATION OF DEFORMITY AND OF REST TO FUNCTION

In the final examination in the residual cases and in the initial examination in all cases we found instances of marked deformity with good function (fig. 3) and of slight deformity with impaired function (fig. 4). There is no constant relation between deformity and function. The average function is less with greater displacement, but this is partly accounted for by greater traumatism in treating them.

Seven patients had two or more months in bed before operation. Their average functional index went up from 30 to 56 before operation and was only 60 in the residual stage. Three were worse after operation. Rest accomplished more in restoring function than did attempts to improve the deformity. One third of the cases in which two and a half or more months were spent in bed became quiescent within four months. All cases with less rest period took longer than this, averaging ten months. These improvements with rest indicate that impairment of function is due in part to inflammation. We believe that it is as important to treat this inflammation as to treat the deformity.

AN OPERATION FOR YOUNG PATIENTS

The seven cases which did not slip were followed to the quiescent or residual stage. None of the four cases relieved of weight bearing during the preslipping stage developed any displacement; of the remaining sixty-six cases, in thirty-one of which a preslipping stage was definitely recognized, only three reached the residual stage without slipping; thus the chance of slipping is great, and two or even three slippings are not infrequent. All cases in which slipping did not occur became symptomless, with normal function. In cases with displacement followed to the residual stage, the index was 46 or less in 50 per cent. To allow displacement to occur is to exchange a potentially normal hip for a 50 per cent chance of having less than 50 per cent function.

In the preslipping cases, slipping must not be allowed to occur. Displacement may be prevented by confinement to bed or possibly by a caliper brace. A brace with weight bearing is of no value in these cases. Such treatment is satisfactory if the patient is old enough to attain ossification of the epiphyseal line in a short while. When the patient is young, an operation to hasten ossification of the epiphyseal disk is better and safer than long periods of bed or brace treatment. Such an operation, used in one case,[1] is as follows: The capsule is opened through a Smith-Petersen incision, and several holes are drilled through the neck and

Fig. 4.—Slight displacement at the left hip with poor function. The index of function was 21.

epiphyseal line into the head. Bone slivers may be inserted in the drill holes. When the patient operated on, a girl, aged 11 years, was up after three months in bed she had an index of 79 and the head was united to the neck (figs. 5 and 6). This was a twenty-point

1. The operation has been used in two more cases since June, 1931, with excellent results to date.

loss in the index representing the effect of operative trauma. We expect this to improve, but a good hip is assured.

That this operation will not cause noteworthy growth disturbance has been demonstrated in cases of coxa plana. For example the earliest of these, done in 1928, shows, in 1931, growth of the neck equal to the

Fig. 5.—Preslipping right hip before drilling was done. The epiphyseal line is wide, the end of the neck is irregular, and the other epiphyseal lines in the region are narrower than on the left.

normal side. The operation has been done in coxa plana fifteen times.

SEQUELAE

Thirty cases that have reached the residual stage were examined roentgenographically for arthritis. None was found in fourteen patients, aged from 12 to 17. Sixteen patients aged from 15 to 27 showed arthritic calcification, most commonly at the margin of the acetabulum; these cases had displacement of from one-fourth to 1½ inches, the average being five-eighths inch. The seven adults showing the late residual of slipped epiphysis all showed arthritic changes. In six it was marked. In unilateral cases the unaffected hip showed no evidence of arthritis.

As all patients over 17 years of age showed evidence of arthritis, we cannot say what will prevent it. It is likely that more attention to rest treatment for the inflammation, treatment of focal infections, general hygienic measures, more efficient reduction of displacement, and prevention of slipping in preslipping cases would improve the results as regards arthritis.

CHOICE OF TREATMENT

Our impressions of the selection of methods of treatment are as follows:

General treatment should include a weight-reducing diet and elimination of foci of infection.

The preslipping case is an emergency case. Weight bearing should be stopped until the disease is quiescent and the epiphyseal line ossified or close to union. If this entails a long period of confinement, it may be better and safer to use the drilling operation.

In the slipping stage, displacements of less than three-eighths inch should be treated as preslipping cases unless very recent, in which case closed reduction might be considered. With more displacement the reduction should be attempted if it is less than two months since the onset of symptoms, less than three weeks since the last displacement, and if callus is very slight in amount. However, if the patient is young there will be danger of recurrence of slipping before the epiphyseal line ossifies, and open reduction with eradication of the epiphyseal cartilage would seem preferable. When cases are not recent, as previously described, open reduction may be attempted if the operator has been successful in obtaining reduction in this way. Otherwise it is best to treat the case by rest until quiescent and then do a subtrochanteric osteotomy, with particular attention to preventing flexion or extension of the proximal fragment. This operation is also the treatment of choice in cases that have reached the residual stage with deformity that interferes with function or predisposes unduly to arthritis.

In all operative procedures, rest from weight bearing should be emphasized. A spica should not be left on more than two and a half months, but there should be no weight bearing for at least three months after operation nor until there is a good range of motion with no spasm except on forced motion. Double spicas are much more apt to maintain reduction than single spicas.

ETIOLOGY

It has been suggested that this disease is due to trauma, static forces, rickets, osteomalacia, infection and endocrine imbalance. In 1926, Key reviewed the literature and did much to refute these theories. The features that we have reported and the cases described in the literature bring us to a conception of this disease which we find helpful as a working hypothesis and guide to treatment. This hypothesis is that weakening at the epiphyseal disk is due to vascular stasis about it secon-

Fig. 6.—Same case as in figure 5 four months after drilling.

dary to sclerotic changes in the soft tissues about the femoral neck. The most probable cause of the sclerotic changes is a previous, or occasionally concurrent, infection—a subacute arthritis or, rarely, infection in the neck. Such infection may be metastatic from infection elsewhere.

Stasis may also be produced in other ways and at other ages, which may account for some related con-

ditions such as coxa plana and osteochondritis dissecans. Transitional cases showing the relation to these other conditions have been excluded from the present report.

This disease is far more common than is generally supposed. Every adolescent child with a hip limp should be examined for it, especially if the child is overweight. If the condition is recognized in the preslipping stage it should be considered an emergency case. Displacement must be prevented. In selecting the treatment to be applied to the given case there must be careful consideration of the age of the patient, the stage of the disease, the presence of callus, and the time since the onset of symptoms and since displacement.

SUMMARY AND CONCLUSIONS

1. Seventy cases of slipping of the upper femoral epiphysis are reviewed.

2. Bilateral occurrence is not infrequent and should always be looked for.

3. Overweight children, whether tall or fat, are more susceptible to the condition. This appears to be due to the greater stress on the hip rather than to any physiologic factor such as endocrine imbalance.

4. Trauma appears to be of importance merely in hastening the onset of symptoms or displacement in a hip which is already diseased.

5. Seasonal variations in onset are accounted for by the seasonal activity of children.

6. The onset of symptoms and of displacement occurs usually during the rapid growth period of adolescence. Exceptions are explained by the factors of weight and trauma.

7. The pathologic features are sclerosis, thickening and avascularity of the soft tissues about the neck, with absence of any primary disease of the bone or cartilage.

8. Sclerotic changes about the neck are followed by a vascular disturbance, resulting in weakening at the epiphyseal disk, which frequently eventuates in slipping.

9. Four stages are described: preslipping, slipping, quiescent and residual.

10. Definite symptoms, physical signs and roentgenographic evidence of the disease are always present in the preslipping stage, and early diagnosis is essential for the best results.

11. After slipping there may be complete incapacitation of the hip or only slight disability, but definite evidence of the condition is always present.

12. Final function is not proportional to deformity.

13. Adequate rest for the hip is the most important factor in obtaining a good result.

14. In hips that have slipped less than three-eighths inch, and in the preslipping cases, rest alone is sufficient treatment. If the period before expected epiphyseal union is longer than six months, drilling across the epiphyseal line will hasten union.

15. (*a*) In hips that have slipped more than three-eighths inch early in the disease and recently, reduction is recommended. (*b*) In later cases with as much displacement, open reduction or subtrochanteric osteotomy after quiescence is advised.

16. In all cases, weight reduction and eradication of foci are indicated.

17. The well developed callus and early union occurring in this condition should be mentioned because of the frequently accepted view that joint fluid interferes with the healing of bone.

18. Arthritis is the usual sequel in adults.

420 East Fifty-Ninth Street.

ABSTRACT OF DISCUSSION

DR. IRVIN BALENSWEIG, New York: I first called attention to this condition in 1926 when, in reviewing a series of cases, I also observed that the end-results were unsatisfactory in patients who were treated by the closed method of reduction. Since that time, further study has led me to believe that this condition, as one sees it in the clinics, has been present anywhere from one to two years prior to the time of observation and that the slipping of the epiphysis is therefore a gradual process except when it is caused by traumatisms, when the head may be grossly displaced. Every attempt should be made to recognize the lesion prior to the slipping; this can be done by subjecting children between the ages of 10 and 12 years to roentgen examination when they present themselves with a history of so-called growing pains in the thighs and an occasional limp. The movements of the hip will be found to be free except those of internal rotation and flexion with the limb in a neutral position; whereas flexion with the limb in external rotation is freer. This sign, to my knowledge, has never been described before. Roentgen examination in these cases reveals a widening of the epiphyseal line, and some fragmentation and areas of absorption in the diaphyseal region. The patients should be treated either by the conservative method of using a Thomas caliper brace or, far better, by a fusion of the epiphyseal line. I am pleased to learn that this type of operation has been carried out at the New York Orthopedic Hospital. It is also wise to roentgenograph hips before and after attempts at reduction in both internal and external rotation. It is only by such a procedure that one can determine the accuracy of the reduction. It is my conviction that when the condition is of long standing reduction cannot be accomplished by manipulative measures.

DR. ALBERT B. FERGUSON, New York: As to the relation to coxa plana, we have a number of cases that we might consider as transitional between coxa plana and slipping epiphysis. Some of these cases resemble, for example, the preslipping stage of slipping epiphysis, but at such an early age we are not sure whether a coxa plana or a slipping epiphysis will develop, and in some, as we followed them, coxa plana has developed, and in others slipping epiphysis has developed. In the paper we have excluded all transitional cases, both those that show a relation to coxa plana and those that show a relation to osteochondritis dissecans. The same applies to cavitation in the neck of the femur. We have a few cases in which actual cavities have been present in the neck and one case in which there was an actual abscess in the neck, which also showed a slipping epiphysis. We consider the latter as a transitional case and have not included it in the report, which is limited to typical cases of slipping epiphysis. The examination of the hip roentgenographically in internal and in external rotation needs to be emphasized, as Dr. Balensweig has brought out. In these closed reductions in which we have reported a very small percentage of success, most of the reductions have been considered good reductions when roentgenographed after the operation. They were found to be anything but good reductions by examination in positions other than the usual anteroposterior position. The patient could be turned on the face in plaster and rotated until the femur was brought into a neutral anteroposterior position or into an externally rotated position, and the displacement would then be visible just as it was before reduction, and, on the other hand, we have made such films, films in internal rotation, which would be the position after reduction. We have made such films before the operation and then had a picture which was exactly the same as the film after reduction. If one wishes to be sure as to the presence or absence of reduction, one must examine these patients very carefully and in several positions. With regard to traction reduction, on the operating table it is, I think, impossible to use the amount of traction which we have used in accomplishing this reduction. It has been demonstrated in these cases that traction of from 300 to 600 pounds (136 to 272 Kg.) in adduction in cases sufficiently recent will reduce the displacement. We have several cases in which the reduction was practically complete and confirmed by views in several directions. We have, however, had considerable difficulty in maintaining that reduction. At least a third and possibly half of the cases in which we have used traction have later showed some displacement, so that we are not yet ready to report on the final result, either anatomically or functionally.

THE NATURE AND ORIGIN OF THE PIGMENTED STREAKS CAUSED BY SEPARATION OF THE CHOROID *

F. H. VERHOEFF, M.D.
BOSTON

It is well known that on ophthalmoscopic examination pigmented streaks are sometimes seen in the fundus in cases in which there has been postoperative separation of the choroid. The streaks are black, have a granular appearance, and may show breaks in continuity. They may be straight or slightly wavy, of various lengths, and quite numerous. Not infrequently they branch. The largest may have about twice the width of a large retinal vein. They are most abundant at the periphery of the fundus, and many of them extend to the limit of the ophthalmoscopic field. Seldom do they reach as near as 2 or 3 mm. to the optic disk. Most of them are more or less meridional in direction and tend to be parallel to one another, but some run in a circular course. In the region of the streaks the fundus may show pale areas and scattered pigment dots. As far as is known, the streaks are permanent. They cause no demonstrable impairment of vision.

The streaks were first described in two clinical cases by Schur [1] in 1913; later Lindner [2] recorded two cases, and Plocher,[3] one case. Schur suggested that folds in the choroid played a rôle in causing them, Lindner that they were due to proliferation of the pigment epithelium such as sometimes occurs after separation of the retina, while Plocher offered no explanation. Fuchs [4] examined microscopically an eye in which separation of the choroid was still present after a perforating ulcer of the cornea. In the choroid he found creases in which the pigment epithelium on one side was in contact with that on the other and assumed that, in cases in which the choroid became replaced, such creases remained and thus explained the black streaks seen ophthalmoscopically. As will be seen later, this explanation was incorrect.

As Fuchs pointed out, these streaks, as seen ophthalmoscopically, differ in important respects from those known as angioid streaks. Especially do they differ in appearance and in the fact that they do not radiate from the optic disk. In spite of these facts, Guist [5] has advanced the view that angioid streaks are due to folds in the choroid, resulting from flat separation of the latter dependent on exudation.

Hitherto the microscopic appearance of the streaks has never been described. Recently I had an opportunity to examine microscopically two eyes in which such streaks were present and five eyes in which separation of the choroid still existed, and I was able to ascertain the exact nature and origin of the streaks. The important features of the cases in which the streaks were found are described herewith. Full details of the other cases are not essential for the purposes at hand and will be omitted.

* From the Massachusetts Eye and Ear Infirmary.
* Read before the Section on Ophthalmology at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 10, 1931.

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5. Guist: Ueber Pigmentstreifen, Ztschr. f. Augenh. **45**: 61, 1921.

REPORT OF CASES

CASE 1.—A man, aged 68, was admitted to the Massachusetts Eye and Ear Infirmary, Feb. 23, 1928, with the diagnosis of chronic congestive glaucoma and bullous keratitis of the right eye. The tension of the eye was 50 mm. Schiötz and its vision was reduced to light perception with faulty projection. The left eye was normal and had normal vision without a glass.

February 24, an iridectomy was performed on the right eye. April 29, the lens was cataractous. July 6, the tension was 45 mm. (Schiötz). The anterior chamber was obliterated. Cataract operation was attempted, but vitreous was lost and the cataract was not removed. Feb. 23, 1929, light perception was still present. The right eye was enucleated.

Pathologic Examination of Right Eye.—The eye was fixed in a diluted "solution of formaldehyde-U. S. P." (1:10) for forty-eight hours, followed by 2.5 per cent hydrochloric acid in a 70 per cent alcohol for twenty-four hours.

The cornea showed pannus degenerativus and marked changes characteristic of old bullous keratitis. The iris below showed marked fibrosis and was adherent to the cornea from its root to the pupil. The capsule of the lens was ruptured and lens matter was bulging the operative wound, which was covered by conjunctiva and a slight amount of connective tissue. The clefts within the lens were invaded by pus cells, many of which were necrotic, and there was a fairly large mass of macrophages with some pus cells between the lens and the cornea—phaco-

Fig. 1 (case 1).—Temporal quadrant of fundus, after fixation and immersion in glycerin, showing typical pigmented streaks. The retina is in situ.

anaphylactic reaction. The anterior part of the vitreous contained a considerable number of swollen cells, apparently chiefly macrophages. Otherwise the posterior part of the eye was free from evidences of inflammatory reaction, except for a few macrophages here and there on the surface of the retina.

The optic disk was deeply cupped. The retina and choroid were everywhere in situ. Ganglion cells were still present in considerable numbers in the macular region but were absent elsewhere. The choroid was everywhere smoothly applied to the sclera. Colloid excrescences were very few in number.

When the eye was opened after fixation, the vitreous was found separated from the fundus by fluid. The fundus showed on each side numerous pigmented streaks identical in appearance with those seen ophthalmoscopically after separation of the choroid (fig. 1). Ten of these were large; eight on one side, two on the other. All except two of these large streaks began near the ora serrata and ran in the direction of the disk, more or less parallel to one another. The largest of these was 9 mm. in length and about 0.2 mm. in greatest thickness. At the posterior end of this was a streak about 13 mm. long running equatorially. Two mm. behind the ora, there was another streak about 5 mm. long, which also ran circularly. The smaller streaks ran in various directions, but mostly either circularly or meridionally. The streaks appeared to consist of coarse pigment dots and showed small breaks in continuity. In the vicinity of the streaks the fundus ofte was paler than elsewhere and showed scattered dots.

Portions of the fundus showing streaks were excised, embedded in celloidin and sectioned as nearly as possible at right angles to the streaks. Before sectioning, some of the blocks were cleared in chloroform, others in glycerin. The streaks could be seen as such while being cut and were therefore definitely identified in the stained sections. One streak was cut for a short distance in serial sections, and another was cut longitudinally for a distance of 3 mm. Microscopically the streaks appeared as well defined thickenings of the pigment epithelium (figs. 2 and 3) and measured from about 0.028 mm. to 0.04 mm. in thickness and from about 0.056 mm. to 0.18 mm. in width. At their sites, the pigment epithelium consisted of from two to five layers of cells densely packed with pigment. The pigment granules retained the spindle form of those seen in normal pigment epithelium. The retina was closely applied to the streaks. In most instances it was slightly bulged up by the streak, but in some instances only its outer layers were compressed by the streak, the inner surface of the retina maintaining its normal level. Occasionally, the surface of the choroid beneath the streak was slightly depressed. In the vicinity of some of the streaks, the pigment epithelium contained somewhat less pigment than elsewhere. In the affected region there were areas, from three to seven cells in width, in which the cells were more densely pigmented than elsewhere and in which there were from one to three pigment cells on the inner surface of the pigment layer.

CASE 2.—A woman, aged 73, with general arteriosclerosis and high blood pressure (240 systolic and 100 diastolic) was first seen at the Massachusetts Eye and Ear Infirmary, Jan. 8, 1930. The vision of each eye was reduced to counting fingers

Fig. 2 (case 1).—Section stained in hematoxylin and eosin, showing a pigmented streak cut transversely. The slight depression of the surface of the choroid beneath the streak may be indicative of the preexistent crease; × 116.6.

at 5 feet. There were numerous scattered retinal hemorrhages in each eye. The tension of each eye was normal.

January 27, the tension of the right eye was 75 mm., that of the left, 17 mm. (Schiötz). The vision of the right eye was reduced to perception of shadows.

January 30, a trephine operation and iridectomy were performed on the right eye, a very large trephine being used.

February 21, extensive separation of the choroid on both sides and below was noted.

November 17, the tension of the right eye was 49 mm., the fundus was not visible and the vision was nil. The right eye was enucleated.

Pathologic Examination of the Right Eye.—The eye was fixed as in the previous case. Sections showed marked sclerosis of the retinal vessels, scattered small retinal hemorrhages, glaucomatous cupping of the optic disk, and peripheral anterior synechia. The retina and choroid were everywhere in situ. There was slight if any edema of the retina. The retinal ganglion cells had entirely disappeared. The lens was not cataractous, but there was a delicate pupillary membrane over it. The trephine wound was covered over with fibrous tissue, which was bulged outward. Serial cross-sections of the central retinal vessels showed complete obstruction of the central vein due to endophlebitis.

When the eye was opened after fixation, the vitreous was found separated from the retina, and the small amount of it remaining was confined to the anterior part of the eye. The fundus showed many pigment streaks on each side, similar to those in case 1. Four of the largest were on the nasal side, each of which began about 4 mm. behind the ora serrata. One, about 10 mm. in length, had a meridional direction; one, about 11 mm. long, ran upward and outward; one, about 12 mm. long, ran downward and, about 1 mm. from its end, the other streak began and continued for about 11 mm. These streaks appeared to be made up of dots, and were about 0.25 mm. in greatest thickness. With the loupe many smaller streaks could be seen. These were irregular or curved, and some of them branched.

Fig. 3 (case 1).—Pigmented streak sectioned longitudinally; × 83.3.

Portions of the fundus containing streaks were excised and sectioned as in the previous case. For a short distance one of the finer streaks was successfully sectioned longitudinally. Microscopically, the streaks were essentially similar in appearance to those in case 1. In this case, however, occasionally a few of the cells in the central portion of a streak were partly or wholly free from pigment (fig. 4). In one instance a colloid excrescence was seen within a streak. This no doubt existed before the streak was formed. The retina was closely applied to the streaks as in case 1, and in all sections made of this eye the choroid was everywhere smoothly applied to the sclera and showed no indentations of the membrane of Bruch. In some areas within the regions of the streaks the pigment epithelium contained less pigment than elsewhere. Over the entire fundus the pigment epithelium showed numerous small colloid excrescences and also other changes which could not be certainly distinguished from those commonly seen in senile eyes.

COMMENT

In neither of these cases were the streaks seen ophthalmoscopically, but as seen with the naked eye and with the loupe, after the globes had been fixed in formaldehyde and opened,[6] the streaks were perfectly typical of those seen after separation of the choroid (fig. 1). The separation of the choroid had been observed

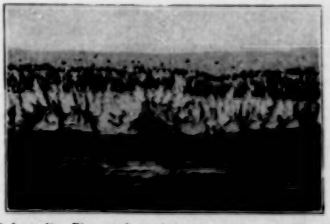

Fig. 4 (case 2).—Pigmented streak in cross-section. In its center is a large cell almost free from pigment; × 116.6.

ophthalmoscopically in case 2 but not in case 1. In case 1, however, two operations had been performed on the eye, the second one seven months prior to enucleation, so that there was an opportunity for the separation of the choroid to have occurred on two occa-

6. As a fixative, solution of formaldehyde has certain disadvantages, but these cases illustrate one of its great advantages; namely, that it permits details in the fundus to be seen almost as well as they can be seen with the ophthalmoscope. After many other fixatives the streaks would have been invisible.

sions. Moreover, as Plocher has pointed out, the streaks are so characteristic that their occurrence is a certain indication that separation of the choroid has previously existed.

Microscopic examination of the streaks in these cases showed that they were situated between Bruch's membrane and the retina proper and were simply ridgelike thickenings of the pigment epithelium (figs. 2, 3 and 4). Occasionally the surface of the choroid beneath a streak was very slightly depressed. It is noteworthy that otherwise the choroid was perfectly smooth, and there was no obvious indication of its having been previously separated, other than the presence of the streaks.

Although apparently having no relation to the streaks, the fact may be worthy of mention here that the vitreous was found separated from the fundus in both of these cases. It is commonly believed that after the separation of the choroid has disappeared the vitreous returns to its normal volume, but these cases seem to show that this is not invariably true. It is possible, however, that the separation of the vitreous antedated the separation of the choroid in these cases.

The question now arises as to the mode of origin of the streaks. To obtain an answer to this, I have

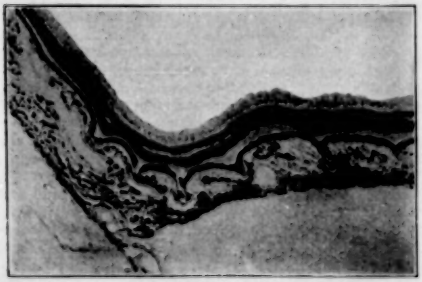

Fig. 5.—Section showing folds and creases involving surface of separated choroid in a case of perforating ulcer of the cornea; reduced from a photomicrograph with a magnification of 36 diameters.

examined sections of the five eyes referred to in which separation of the choroid still existed. In one eye the separation was due to a recent perforating ulcer of the cornea; in the others the separation had occurred without an obvious cause.

In each of these eyes the choroid showed folds of various sizes, but they were more numerous in the eye with the perforating ulcer. The choroid and the retina together were involved in large wavelike folds, but only their inner surfaces showed small folds and creases. The small folds of the choroidal surface were rounded and inward, i. e., toward the retina, while the creases were between the folds and much sharper (fig. 5). As seen in the sections, the creases appeared as indentations, which involved chiefly the pigment epithelium, Bruch's membrane and the choriocapillaris. In some instances the pigment epithelium did not take part in the crease but bridged it over. In some of the larger creases the pigment epithelium was partly absent, partly depigmented or otherwise altered. In a few instances the epithelium on one side of a deep crease was in contact with that on the other side, as Fuchs described. In a few of the creases, the spaces within them were partly or completely filled with pigment cells evidently derived by proliferation of the original pigment epithelium (fig. 6). Probably in these the portions of the epithelium on each side of the creases had been for a time in contact and had fused together, and later the creases widened, thus causing the pigment cells to pro-

Fig. 6.—Section from same eye from which figure 5 was obtained, showing a crease filled with pigment cells. When the choroid becomes reapplied to the sclera, the pigment cells in such creases are lifted up so as to form pigmented streaks; × 111.

liferate and fill the resulting spaces. From one of the eyes a segment of the separated choroid was excised and the retina peeled away from it. With a loupe, pigmented streaks could then be plainly seen on the choroidal surface (fig. 7). One streak branched into two at one end. The streaks were more numerous and much thinner than those seen in cases 1 and 2 (fig. 1), in which the choroid was in situ. The largest measured 0.02 mm. in width. A portion of the segment was then reembedded and the streaks were sectioned transversely. The sections showed definitely that the streaks were fine creases such as shown in figure 5.

These fine pigmented streaks (creases) that exist while the choroid is still separated are not generally observed on ordinary ophthalmoscopic examination, no doubt because the separated choroid is poorly illuminated and appears dark. In a recent case, I was unable to see them when illuminated by the ophthalmoscope but could see them plainly, and also recognize folds in the choroid, when the latter was strongly transilluminated through the sclera.

Fig. 7.—Segment of the separated choroid, from which the retina has been peeled, in a case of spontaneous separation of the choroid. The pigmented streaks are more numerous and much finer than those seen after the choroidal separation has subsided (fig. 1) and correspond to creases such as are shown in figures 5 and 6.

The explanation of the formation of the folds and creases is probably as follows: Separation of the choroid is due to the fact that the pressure in the vitreous chamber has become less, for a time, than that in the perichoroidal space. As the choroid separates it is, with the retina, for obvious reasons, forced into folds. The two structures are also at the same time compressed into a smaller surface area than they originally occupied. The outer parts of the choroid and retina, being relatively soft, yield to the compression usually without folding further, but the membrane of Bruch with the choriocapillaris and the inner surface of the retina, owing to their greater rigidity, are forced

into rounded inward folds associated with outward creases.

From the foregoing observations the manner in which permanent pigmented streaks are formed as a result of separation of the choroid is now apparent. When the choroid is reapplied to the sclera, it is stretched to its original dimensions, so that all the folds and creases entirely disappear, leaving its surface smooth. As a result, the pigment cells that had accumulated in some of the creases are lifted up in the form of ridges on the surface of the choroid, visible with the ophthalmoscope as pigmented streaks. At the same time, the retina is smoothed out and is closely applied to the streaks.

The granular appearance of the streaks is due to the fact that the accumulations of pigment cells were not uniform throughout the creases, and the irregularities and breaks in the streaks correspond to similar defects in the preexistent creases.

The paler areas sometimes seen in the affected portion of the fundus are due to diminution in the amount of pigment in the pigment epithelium, resulting, no doubt, from the abnormal conditions of nutrition existing while the choroid was separated. The discrete pigment dots, separate from the streaks, are due to increased pigmentation and proliferation of the pigment epithelium in small areas, possibly corresponding to small pits which existed in the surface of the separated choroid.

The reason that the streaks do not occur near the optic disk is that the choroid is so firmly united with the sclera in this region that it seldom if ever becomes separated here.

As to the frequency of their occurrence, it might be supposed, judging by the scarcity of the recorded cases, that these permanent streaks are extremely unusual. But it seems to me, nevertheless, that they may be of relatively frequent occurrence and are often overlooked. I have seen them in very few cases but am sure that I have not always examined the fundus, especially its periphery, with sufficient thoroughness to detect them. It is certain, however, that they do not occur in every case in which there has been separation of the choroid. Obviously, they would not be formed in cases in which the separation was of short duration, for the observations here recorded clearly indicate that the extent and duration of the separation are determining factors in their formation.

As to the time when the pigmented streaks are formed, the cases recorded in the literature afford no exact information. Lindner observed the streaks in his second case three days after the separation had subsided. But in this case a trephine operation had been performed three months previous to the final operation, so that the streaks may have occurred then and have been overlooked. Plocher discovered streaks in his case two months after the separation was first noticed, and before it had entirely subsided. The actual observation, by means of a loupe, of pigmented streaks on the surface of the separated choroid in one of the present cases (fig. 7), as previously described, shows that streaks actually exist before the separation has subsided. These streaks, however, are much finer and more numerous than those seen in cases in which the choroid has become replaced (fig. 1), and sections made of them show that they are really fine creases (fig. 5). They are not generally recognized on ordinary ophthalmoscopic examination, but, as previously noted, in a recent case I was able to see them by transilluminating the separated choroid through the sclera. No doubt, when the separation subsides and the creases have been smoothed out, all the streaks disappear except those in which pigment cells have accumulated. The permanent streaks, actual ridges of pigment epithelium, must certainly appear soon after the choroid has been reapplied to the sclera.

In a previous communication before this section, I[7] demonstrated the nature and origin of angioid streaks, showing that the latter are corrugations of the inner surface of the choroid, including the pigment epithelium, resulting from fibrosis of the outer layers of the choroid. From the observations that I have recorded, it can now be regarded as certain that the pigmented streaks resulting from separation of the choroid are entirely different in nature and origin from angioid streaks.

CONCLUSIONS

From macroscopic and microscopic studies of two eyes showing pigmented streaks in the fundus, and of five eyes in which separation of the choroid still existed, the following conclusions are drawn:

Pigmented streaks in the fundus resulting from separation of the choroid are entirely different in nature and origin from angioid streaks.

Very fine pigmented streaks exist while the choroid is still separated. These are furrow-like creases in the surface of the choroid. They are not usually visible on ordinary ophthalmoscopic examination but they may be seen, in some cases at least, by transilluminating the separated choroid through the sclera. All these creases disappear as such when the separation subsides.

The permanent pigmented streaks, seen after the separation has subsided, are ridgelike thickenings of the pigment epithelium.

The pigment cells composing the permanent streaks originally accumulate within some of the furrow-like creases that exist while the choroid is separated. When the choroid becomes reapplied to the sclera and these creases are smoothed out, the accumulations of pigment cells are elevated, thus giving the appearance of streaks.

82 Commonwealth Avenue.

ABSTRACT OF DISCUSSION

DR. T. B. HOLLOWAY, Philadelphia: As Dr. Verhoeff has stated, the recorded case histories of pigmentation after detachment of the choroid are rare, and it is gratifying that these cases should have come under his observation and that his observations are available for this section. The only probable case of this character that I have seen was in an eye observed at the former Polyclinic Hospital, fourteen or fifteen years ago, and at the time the significance of the pigmentation was not understood. In character it corresponded to the type under discussion. It was not until I had occasion to review the literature concerning angioid streaks and saw references to this type of pigmentation developing after choroidal detachment that the case mentioned was recalled. Naturally, those who have described these cases have pointed out those characteristics that differentiate them from angioid streaks, or, as Verhoeff has suggested, fibrosis choriodeae corrugans. Nevertheless, it is interesting to note that each of these types of linear pigmentation has to do with the pigment epithelium, the one doubtless of vascular origin, with fibrosis, as the author has shown, as the contributing factor, while in the other case it is brought about as the result of what might be regarded as a mechanical sequence of a detached choroid. While it has been shown that these streaks may be visible with the ophthalmoscope within a few days after the choroid has become detached, Dr. Verhoeff

7. Verhoeff, F. H.: The Nature and Pathogenesis of Angioid Streaks in the Ocular Fundus, Tr. Sect. Ophth. A. M. A., 1928, p. 243.

has pointed out the more important fact that by the use of transillumination they may be observed during the period of detachment. This simply means that in a case of choroidal detachment the eye must be examined by transillumination as soon as it is permissible. If the author's belief in regard to the character of the cases with which he was dealing is accepted, there is little use to speculate as to theories when confronted by definite pathologic observations.

DR. E. V. L. BROWN, Chicago: One characteristic of the detachment streaks was not sufficiently stressed or discussed by Dr. Verhoeff, although definitely present and described in each of his cases; namely, their predominantly longitudinal and circular course. It seems to have been present in practically all other reported cases. There are two kinds of pigment streaks in the fundus, the angioid streaks and streaks due to detachment of the choroid, both due to changes in the choroid, the pathology of each of which Dr. Verhoeff has definitely established. There is a third kind which apparently is rare, or at least concerning which little has been written; namely, the kind due to arteriosclerosis of the choroidal vessels. This was first described clinically in two cases (and anatomically in one of the cases) by Siegrist in 1899. I would suggest a new explanation of these streaks; namely, that the streak or ridge formation is possibly due to inward pressure of certain larger choroidal vessels against the pigment epithelium. This pressure would bend the lamina basalis inward in a weakly convex curve just over the course of the vessel. Siegrist specifically notes that both ophthalmoscopically and anatomically there were no streaks over the completely sclerosed vessels; perhaps complete hardening took place in arteries only or in small veins and thus made no bending inward of the lamina basalis. His drawing shows only small vessels sclerosed, only larger ones with pigment. Possibly these larger vessel walls first become relaxed as described by Thoma decades ago, then distended, and press gently but constantly against the lamina and epithelium, like a tight shoe on a corn, and make the epithelium proliferate just along the line of pressure.

DR. F. H. VERHOEFF, Boston: I am aware, of course, that pigmented streaks sometimes result from separation of the retina, and I have seen them in cases of high myopia and other conditions; but such streaks occur so rarely and are so scanty when they do occur that they do not properly come within the scope of my paper. With the streaks described by Siegrist, however, I was unacquainted until his paper and that of Koeppl were called to my attention by Dr. Brown a few days ago. These streaks have no relation to postoperative separation of the choroid, but they are pertinent to my paper because they are histologically similar to the streaks investigated by me. Siegrist could offer no satisfactory explanation for their occurrence. Three possible explanations in addition to those offered by him suggest themselves to me: First, that they are due to antecedent, spontaneous separation of the choroid. Against this are the facts that they appear close to the optic disk, where separation of the choroid almost never takes place; that they follow the course of the choroidal vessels and have a definitely beaded appearance. Second, that they result from previous creases in the choroid. Against this is the difficulty of explaining how sclerosis of the choroidal vessels could cause such creases. Creases are shown in Siegrist's illustration, but they are probably artefacts dependent on postmortem changes. Third, that the streaks are caused by pulsation of certain choroidal vessels. When there is marked sclerosis of the choroidal vessels, it is reasonable to assume that for a time some of the latter may pulsate to an unusual degree and that the pulsation may locally stimulate the pigment epithelium to proliferate. Siegrist found, both ophthalmoscopically and microscopically, that the streaks occurred only in relation with thin-walled vessels. Against this explanation are the facts that such streaks are beaded and occur very rarely, but nevertheless at present it seems to me the most probable one. In regard to Dr. Holloway's comment about overlooking streaks, in the case in which I found creases I later had the patient come back and then found three large streaks in the lower inner quadrant, three in the upper outer quadrant, and a number of small ones. These streaks had not been seen on several other visits to the clinic, because a special effort had not been made to find them.

THE PREVENTION OF GOITER IN DETROIT AND CLEVELAND

O. P. KIMBALL, M.D.
CLEVELAND

The comparative study of the prevention of goiter in Detroit and in Cleveland demonstrates how quickly any community can completely eradicate endemic goiter when there is a unity of all the forces that direct its public health. Without this unity, public health cannot take care of itself. The safety of present methods of prevention of goiter also is considered.

Detroit and Cleveland are practically the same size, and as far as is known the natural conditions and the factors determining endemic goiter are the same. I have been intimately connected with the work in the two cities. In Detroit this preventive measure had the leadership and cooperation of the state department of Health, the city department of health, the school board, school physicians and the medical profession. In Cleveland there has been no unity of thought or action.

The Michigan State Department of Health, after surveys determining the incidence of goiter and the iodine content in the various water supplies throughout the state, early in 1924 outlined a definite program for goiter prevention. They decided on the use of iodized salt. A conference with the salt manufacturers and later with the wholesale grocery men was held, resulting in a definite cooperative plan that only iodized salt would be used as food in Michigan. Iodides have always been expensive, costing around $3 a pound even when bought in large quantities. To prevent an increase in the cost of salt, which might be used as an argument against the use of iodized salt, the manufacturers agreed to stand half of the increase in the cost of production, and the wholesale grocers the other half, thereby keeping the cost to the consumer the same as that of ordinary table salt. It was further agreed that the state department of health would do all the educative work, making advertising by the salt producers unnecessary. Under this plan iodized salt was put on the market throughout the state of Michigan in May, 1924.

A survey had been made in the Detroit schools in the winter of 1924, so that the incidence of goiter just preceding this prophylactic movement was fairly well established. This survey was outlined and directed by me with the assistance of two physicians who had worked with me, thus insuring uniform data. One of these physicians, Dr. Gudakunst, has been director of health education in the schools and has continuously emphasized the prevention of goiter. Further, the Detroit school board ordered the purchasing department to use only iodized salt in their cafeterias, which feed 50,000 children daily.

In Ohio the state department of health became interested and in 1925 appointed me as consultant on goiter to the state health department, for the purpose of carrying out a survey in various sections to determine the incidence of goiter and institute a definite program of prophylaxis. To this end in the fall of 1925 all the children in two counties in the southern section of the state, in two in the central section and two counties along the lake were carefully examined. Altogether, 60,000 school children were examined for thyroid enlargement. We planned to concentrate the efforts of the state department of health in these counties, expecting to be able to control the situation so that only iodized salt would be used. Then

satisfied with these observations, I gave the formula to other surgeons and asked for unbiased reports. The reports were all enthusiastically commendatory, and it is after a test period of over eight years that the formula and technic are now to be published.

The technic of application here described is the means of securing the maximum result by the use of the formula.

The formula, which has been called oxyquinoline sulphate scarlet R ointment, is as follows:

		Gm. or Cc.	
℞	Oxyquinoline sulphate	16	gr. x
	Chlorbutanol (choretone)	2.4	gr. xl
	Liquid petrolatum	4.0	ʒ i
	Scarlet R ointment, 5 per cent	120	ʒ iv

When 10 per cent scarlet R ointment is used, take 2 ounces and petrolatum, 2 ounces.

The oxyquinoline sulphate and the chlorbutanol are ground separately into fine powders and then mixed separately with portions of the liquid petrolatum. All the ingredients are then made into a red ointment. The finished ointment is heated until fluid, and rolled gauze bandages, 32 by 44 mesh, or coarser, are immersed in the hot ointment until the entire bandage is thoroughly impregnated, until all bubbling has ceased. When cool, it is ready for use. The finished product has been called oxyquinoline sulphate scarlet R gauze.

The formula herewith presented will impregnate completely three 10-yard gauze bandages, 2 inches wide, or six, 1 inch wide, provided it is heated in a small vessel; for example, an aluminum measuring cup such as is ordinarily used in the kitchen.

When a bandage has been immersed in the ointment as described, the mesh of the outer layer or two is covered completely and these layers are discarded. The warp and woof of the rolled gauze are completely impregnated with the red ointment, but the interstices are open. A bandage so prepared will keep indefinitely if contamination is avoided.

The rationale of the ingredients is easily given.

Oxyquinoline sulphate is a definite chemical compound. It is a yellow crystalline powder, a powerful antiseptic, nontoxic, and it does not destroy growing cells. It does not coagulate albumin or injure mucous membranes. In this ointment its strength is as 1 to 200.

For over twenty years I have applied oxyquinoline sulphate powder to wounds by means of cotton tipped applicators wet with alcohol and have found it a most valuable application for preventing and overcoming early or potential infections.

Chlorbutanol, trichlortertiarybutyl alcohol, is a definite chemical compound having marked local anesthetic properties and is mildly antiseptic.

Scarlet R ointment containing 5 per cent Scarlet R Medicinal Biebrich is definitely stimulating to the epithelium and promotes its growth. This dye is a definite chemical substance, aminoazotoluenеazobetanaphthol. This preparation has enjoyed wide use for many years, but its value is greatly increased by the formula here presented.

Dimazon, diacetylaminoazotoluene, has been used in place of the scarlet R, but the results seemed more satisfactory with the red ointment.

The application of oxyquinoline scarlet R gauze to the wound is very simple. Excess secretions are removed by gently but firmly pressing with dry gauze. When cotton is used on wounds, small bits adhere. Short pieces of oxyquinoline scarlet R gauze are cut and laid directly on the wound, completely covering the entire surface with but a single layer. Overlapping is reduced to a minimum. Dry gauze is then applied in sufficient thickness to carry away the secretions and to protect the wound. A bandage keeps the red gauze in close contact with every part of the wound surface.

The dressings are changed every second to fifth day, care being taken that the new epithelium is not disturbed. The dressings usually come away readily. When they do not, which is rare, they are left until the next dressing and are never pulled off. Frequently the red gauze is left in place until complete epithelization has occurred.

Infection slows up the normal rate of wound healing, and when infection is eliminated healing goes on with surprising rapidity. By the use of this method the healing time is greatly shortened, resulting in soft scars with less tendency to bind and, therefore, a minimum of deformity. Healing is rapid and the wound is clean throughout.

When ointment is applied to gauze as one spreads butter on bread, the mesh is closed in the center by a thick layer and the edges are devoid of ointment. The application of such a dressing holds the secretions in at the center and allows the dry gauze at the periphery to stick to the wound. When secretions are held in contact with a wound, the tissues beneath are broken down. When secretions are carried away, this breaking down does not occur.

Lest it be misunderstood, let it be distinctly stated that the formula and method here described are not a primary treatment for burns. The best results as first treatment of burns are obtained by using tannic acid and forced fluids. The treatment here described is for the healing of the resulting ulcerated surfaces.

An important use of this dressing is in preparing wound surfaces for skin grafting. The application of oxyquinoline scarlet R gauze will rapidly clean up infected granulations and make them ready for Thiersch or other skin grafts. The application of this gauze for three or four days is often sufficient. Following Thiersch or Reverdin grafting, the gauze is applied over the grafts, and the dressing is not changed for four or five days or longer. Rapid healing minimizes the formation of scar tissue between grafts. Chronic ulcers of the leg, x-ray and radium burns, and other sluggish processes respond readily.

When oxyquinoline scarlet R gauze is used, skin grafts will take very frequently where otherwise they would not. It is during the waiting period while the denuded area is being made ready for skin grafting that scar tissue with its resulting contractions is increasing. By the use of this method, skin grafting can be done early and disfiguring contractions and webbings prevented.

Dressings are changed less frequently when oxyquinoline scarlet R gauze is used. Every fourth, fifth or sixth day the entire dressing is removed, while every second to fourth day the outer dressings may be changed. By replacing the outer dressings as necessary, the mesh in the oxyquinoline scarlet R gauze is kept open, and the new dressings carry away the drainage.

The application of a very thin layer of the ointment is made occasionally directly to healing incisions and is an aid to the production of invisible scars.

A boy, aged 9 years, received an extensive burn extending from the umbilicus to the left ankle. The entire skin surface sloughed, leaving an ugly, weeping wound. The immediate treatment with tannic acid and

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forced fluids was satisfactory, but under several later treatments he was most uncomfortable and required frequent narcotic medication. Within thirty minutes after the application of the oxyquinoline scarlet R gauze, he went to sleep without a narcotic.

An elderly man had a chronic ulcer of the leg, which resisted healing, although many types of treatment had been used. Under the application of oxyquinoline scarlet R gauze, the lesion was healed in two weeks.

An elderly woman received an x-ray burn involving an area 7 by 4 inches. Before I saw the patient, various treatments, including skin grafting, were tried over a period of eight months, without lessening the size of the wound in the slightest degree. The application of this gauze to the area healed it completely. The healing was progressive from the very start, a slow advance being noticeable from day to day. The resulting scar is soft and pliable, and there are no heavy bands and no contraction.

This report is made with confidence that those who use oxyquinoline scarlet R gauze as herein described will reap the satisfaction which I and those of my colleagues who have been using it have had.

629 Medical Arts Building.

THE CAUSE AND PREVENTION OF RADIODERMATITIS *

H. H. HAZEN, M.D.
WASHINGTON, D. C.

This study of 111 cases of radiodermatitis following the application of either x-rays or radium is based on patients seen in private practice. The cases are consecutive but include only those in which the total dosage can be estimated either absolutely or with a very fair degree of accuracy. Cases occurring as the result of high voltage therapy for malignant diseases of the breast, thorax or abdomen are not included, nor are instances in which a few telangiectases have appeared in a limited area following the treatment of skin cancer; nor is reference made to fibrosis of the lungs, or intestinal injury as the result of intensive irradiation.

Of these 111 cases, 40 occurred in men and 71 in women. Three resulted from the taking of roentgenograms; thirteen from high voltage therapy; seven

TABLE 1.—*Years During Which Treatment Resulting in Radiodermatitis Was Received*

Years	Number of Cases
1910 to 1912	8
1913 to 1915	17
1916 to 1918	21
1919 to 1921	18
1922 to 1924	11
1925 to 1927	19
1928 to 1929	17

occurred in roentgenologists; thirteen were from treatments received in beauty shops, and the remainder, or seventy-five, from superficial therapy. Eight cases were the result of high voltage therapy by dermatologists and fifty-eight of low voltage therapy by dermatologists, while five were from high voltage therapy by roentgenologists and seventeen from low voltage therapy by roentgenologists. Table 1 shows the years when treatment responsible for the radiodermatitis was received.

When it is remembered that thirteen patients were damaged in beauty shops between 1927 and 1929, it will be noted that the number of cases of radio-

TABLE 2.—*Location of Radiodermatitis*

Part of Body Affected	Number of Instances
Face	38
Neck	15
Hands	20
Feet	8
Body	13
Arms or legs	12
Scalp	11
Scrotum	3
Perineum	4
Gums	7

dermatitis attributable to physicians is decreasing. This is probably a just estimate, as the majority of operators know better the limitations of radiotherapy. Of these 111 cases, 7 were from radium and the remainder from x-rays.

There has been a prevailing impression that radiodermatitis is usually manifest by the end of the first year and that it invariably appears before the end of the second year. In this series of cases, ninety-seven patients showed signs of injury before the expiration of twelve months, and an additional eight before two years had elapsed. Four cases showed nothing for three years, and in two instances the first signs of

TABLE 3.—*Character of Injuries*

Type of Injury	Number of Instances
Depilation	6
Permanently dry hair	5
Localized dryness	2
Atrophy and wrinkling	6
Telangiectases	78
Keratoses	14
Acute second degree burns	5
Third degree ulcers	14
Injury to gums	7
Sclerosis of muscles	1
Cancer	4

trouble appeared after forty-eight months. There are a few cases on record in which the appearance of telangiectasis has been delayed even beyond this period.

The location of the radiodermatitis is shown in table 2.

It should be noted that many patients showed a radiodermatitis in several areas, which fact is responsible for the divergence in figures.

The character of the injuries is shown in table 3.

Of the third degree lesions, nine were due to treatment received from roentgenologists and five from dermatologists.

Regarding the character of the lesions, there is space for only a few words. Five cases of permanently dry hair occurred in children from an institution where ringworm had been epidemic for years. These children were depilated either four or five times, and two years after the last depilation the hair was rather scanty, thin, dry and partially white. Three of the cases of depilation were the result of roentgenography and the other three resulted from therapy. The injury

* Read before the Section on Dermatology and Syphilology at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 12, 1931.

to gums has already been discussed by me,[1] in an article, "Injuries Resulting from Irradiation in Beauty Shops."

The conditions for which x-rays were given are listed in table 4.

TABLE 4.—*Conditions for Which Treatment Was Given*

Condition Requiring Treatment	Number of Cases
Acne	16
Superfluous hair	14
Psoriasis	4
Pruritus ani	4
Dermatophytosis	9
Tinea tonsurans	7
Tinea cruris	3
Warts	8
Dermatitis venenata	4
Lichen planus	1
Cancer	4
Keloid	5
Nevi	3
Lupus vulgaris	3
Tuberculous glands	4
Thyroid hypersecretion	5
Superficial nodules	2
Sarcoma	2
Excessive menstruation	2

Table 5 shows the location of the third degree burns, and the condition for which treatment was given.

TABLE 5.—*Third Degree Burns*

Condition Requiring Treatment	Number of Cases	
Lupus vulgaris of face	2	
Pruritus ani	2	
Dermatophytosis of foot	2	
Wart on hand	1	
Cancer of ear	1	(radium)
Sarcoma of jaw	1	
Sarcoma of axilla	1	
Excessive menstruation	2	

The location and primary conditions of the cases which resulted in serious keratoses are listed in table 6.

TABLE 6.—*Cases Resulting in Serious Keratoses*

Primary Condition	Number of Cases
Superfluous hair of face	1
Superfluous hair of legs	1
Psoriasis of feet	1
Psoriasis of legs	1
Dermatophytosis of foot	1
Wart on hand	1
Linear nevus of hand	1
Lupus vulgaris of face	1
Dermatitis of face	1
Industrial exposure in roentgenologists	5

It is to be noted that many patients suffering from comparatively benign conditions were among those who were most seriously damaged.

The patients mentioned in the foregoing lists met with the fates shown in table 7.

Of the 111 patients, 37 had been treated with rays filtered through 1 to 3 mm. of aluminum, and the remainder with unfiltered rays. These figures are of little value, as they fail to show the total number of patients treated with either filtered or unfiltered rays in whom no permanent injury developed. The attempt was made to learn whether various voltages had the slightest effect. So far as could be deduced in this series of cases, there was no difference in results of patients treated with a peak voltage of 80 or of 130 kilovolts.

1. Hazen, H. H.: Am. J. Roentgenol. **23**: 409 (April) 1930.

It has also been stated that the face, neck, flexor surface of the arms, and the skin covering the joints are unusually susceptible. In seven patients the same dosage was given to the skin of the face, and either to the shoulders, arms or legs; the resultant injuries are practically the same in all places, which would tend to show that there is comparatively little difference in susceptibility of the skin in various areas. However, it should be noted that telangiectases did not develop on the back of the hands unless the total amount of rays received was in excess of 6 units, so it is evident that this portion of the body is unusually resistant.

In twelve persons, telangiectases developed without any preexistent erythema. But a few years ago the teaching was that such an event could never take place without an erythema following treatment. However, if one will recall that many roentgenologists have had telangiectases which developed from the cumulative effect of many tiny doses, the falsity of this teaching

TABLE 7.—*End-Results of Roentgenography and Roentgenotherapy in Some Cases*

Result	Number of Cases
Death from cancer of face	1
Amputation of arm	1
Amputation of leg	1
Amputation of fingers	3
Extensive skin graft to hand	1
Extensive skin graft to feet	2
Extensive skin graft to body	2

should be apparent. All twelve of these patients had been under close observation by competent men, and an erythema could scarcely have escaped attention. Two of the patients had received a total dosage of only 3 units; two had received a dosage of 4 units; four a dosage of 5 units, and the remainder a dosage between 5 and 6 units. It is worthy of comment that the patients in whom dilated vessels developed after a total dosage of but 3 units were both women with excessively dry skin.

While this series of cases is comparatively small, it would seem obvious that a total dosage of 2½ units is all that can be safely administered to a patient with a very dry skin, and a maximum of 4 units to a patient with a normal skin. This is an important observation, as it tends to establish the total dosage that can be administered to any one patient over a period of years.

As patients can stand only a definite total amount of irradiation, it is absolutely incumbent on the radiologist to learn just what dosage has previously been received. Likewise, in estimating the total dosage which has been applied to the face, the number of dental roentgenograms should also be taken into consideration. When a patient has had from fifteen to twenty roentgenograms of the teeth taken, the total amount of x-rays received is not small.

Excluding the patients who were damaged in beauty shops, it was found that twenty-eight patients received their injuries from one heavy dose of from 1 to 3 units; sequelae developed in fifty-one after repeated heavy doses of from one-half unit up, and eighteen showed radiodermatitis after fractional treatments in which no dose was over one-fourth unit.

Another important point is that only seven patients showed sequelae when the diameter of the area treated was less than 1 inch (2.5 cm.). It is a well known fact that an area not more than one-fourth inch (0.6 cm.) in diameter will stand a total amount of treatment that

would utterly destroy tissue in an area of 2 or more inches. To determine how much irradiation small areas will stand, a survey has been made of 250 cases each of cancer and of warts, and the following are the facts for unfiltered therapy:

Area, one-fourth inch diameter: A single dose of 3 units or a total dosage of 9 units, provided that no irritating substances are used or that subsequent dosage is not repeated in the presence of an erythema, will cause a little atrophy but no other sequelae.

Area, one-half inch in diameter: The results are the same as noted in the preceding paragraph, except that telangiectases will appear in 10 per cent of the cases.

Area, 1 inch in diameter: Single doses of 2 units, or a total of 6 or 7 units, will result in some atrophy and a few telangiectases in 15 per cent of all patients.

Area, 2 inches in diameter: Single doses of 2 units, or a total of 6 units, will show considerable atrophy and some telangiectases in nearly all cases.

In the light of our present knowledge, certain of the patients were unsuitable for irradiation. In this group should be placed thirteen patients with hypertrichosis who were injured in beauty shops; two patients with hypertrichosis of the nucha; three with tinea cruris involving the scrotum; one with primrose dermatitis; three with large pigmented nevi, and two with lupus vulgaris and extensive scar formation in which the pathologic changes already closely resembled those found in a chronic radiodermatitis. In addition, the patients with keloids should have been permitted a long interval between treatments to allow for late shrinkage of the lesions, and the patients presenting tinea tonsurans should not have been depilated more than three times.

Regarding the causes of radiodermatitis it is probable that the list shown in table 8 is as accurate as possible at the present time.

TABLE 8.—*Causes of Radiodermatitis*

Causative Factors	Number of Instances
Handling radium with fingers	1
Meter out of order	9
Meter maladjusted	1
Omission of filter	1
Patient went to sleep and did not remove radium	1
Too many epilations (tinea tonsurans)	5
Movement of patient with tinea tonsurans	1
Timer stopped	1
Deficient timer	1
Too large areas for heavy dosage	5
Irritant drugs used by patients	5
Patients taking treatments from several physicians	5
No filter on radium	4
Protection slipped	1
Too many or too heavy treatments	69

It is probable that strict observation of the following points would eliminate many cases of radiodermatitis:

1. Patients should be carefully selected. Pigmented nevi should be treated with x-rays or radium only after careful consideration, as destructive doses are necessary.[2] The mild type of acne should be treated with x-rays only as the last resort; patients troubled with constipation or young patients should not be treated. Pruritus ani should be treated with irradiation only when all other methods have failed. Lupus vulgaris with extensive scarring already has pathologic manifestations similar to radiodermatitis and hence should be treated with the utmost caution. Dermatophytosis in the majority of instances will yield very much better to other forms of therapy than it will to irradiation. Warts, except plantar warts, are better treated by desiccation than by irradiation. Psoriasis,[3] because of its certainty to relapse and its chronicity, should be irradiated with the utmost caution. Keloids[4] frequently continue to shrink for three or four months with a unit or a unit and a quarter dose; hence treatment of keloids should be given at long intervals.

2. The apparatus should be modern. There should be two miliammeters, or the milliammeter should be standardized at least once every two months. The timer should be accurate and properly controlled. The apparatus should be standardized as to dosage; the best method is epilation of scalp hair.

3. The use of irritating drugs must be avoided by the patient who is receiving roentgen treatment. MacKee[5] has called attention to the fact that such drugs as iodine, phenol (carbolic acid), salicylic acid, the mercurials and all stimulating preparations are very prone to set up a dermatitis when used in conjunction with x-rays. Therefore the patient should never use any drug over an irradiated area without the knowledge and consent of the radiologist.

4. The patient should not take roentgen treatments from a number of physicians at the same time. It is perfectly amazing, but I have known at least one patient who was irradiated by three different physicians at the same time without any of the radiologists being aware of this fact. The patient should be educated, or at least instructed, never to seek roentgen treatments without giving the names of the men who have previously treated him.

5. Radium should always be filtered through either rubber or aluminum.

6. As small fields as possible should be used if heavy doses must be employed.

7. Fractional doses are much safer than quantities approaching erythema doses.

8. Erythema doses should always be avoided except in malignant conditions or in warts.

9. In the treatment of ringworm on scalps of institutional children, not more than three epilations should be done.

10. Dry skins should never have a total of more than 2½ units even over a period of years.

11. Ordinary skins should not have a dose of over 4 units, and very greasy skins not over 4½ units.

1911 R Street.

ABSTRACT OF DISCUSSION

DR. ANTHONY C. CIPOLLARO, New York: The cause of acute x-ray injuries and of x-ray sequelae is overdosage. Dr. Hazen discussed many of the causes of and reasons for excessive dosage. In general these causes may be divided into technical errors and errors of judgment. While modern technic is by no means scientifically accurate, it has stood the test of time in practical therapy and it is absolutely safe for therapeutic purposes when employed with skill, care and judgment. Dr. Hazen said that telangiectasia occurs without antecedent erythema. I admit that the statements may be true, but I doubt that it is so. Dr. MacKee, in twenty-five years, has not seen a single instance of telangiectasia in which he was absolutely certain that a previous erythema had not occurred. So far as the size of the exposed surface is concerned, the biologic effect increases with the size of the surface until the area is 4 inches square, after which the increase in the size of the exposed area does not

2. MacKee, G. M.: X-Rays and Radium in the Treatment of Diseases of the Skin, ed. 2, Philadelphia, Lea & Febiger, 1927, p. 639.

3. Hazen, H. H.: South. M. J. **22**:932 (Oct.) 1929.

4. Hazen, H. H.: Am. J. Roentgenol. **11**:547 (June) 1924.

5. MacKee, G. M.: X-Rays and Radium in the Treatment of Diseases of the Skin, p. 270.

matter. The difference in the effect on an area 1 inch square as compared with an area 4 inches square is approximately 25 per cent. This is due to scattering of the rays by the tissues and also to secondary rays. I gather that Dr. Hazen does not believe that variation in individual and in topographic toleration is important. It may not be a major cause, but I believe that it is important. I shall call attention simply to the fact that an epilating dose applied to the scalp will evoke defluvium but not erythema; the same dose applied to the face will often effect erythema without causing alopecia. I do not agree that it is unsafe to give more than a total of 2½ units to dry skin, but I do believe that dry skin is at times less tolerant than is oily skin. The same is true of an inflamed or a florid skin. I desire to emphasize the importance of making the technic as accurate as possible. The dermatologist must not rely solely on the advice of the manufacturer or even on that of the physicist. He should obtain the help of the physicist by all means, become proficient in the use of instruments of precision, such as the voltmeter, the milliamperemeter, the spark-gap, the selenium cell intensimeter, the dosimeters based on ionization, and so on, obtain instruction and advice from reliable practical sources, study reliable textbooks and, finally, depend on skin effects. The modern ionization dosimeter is an excellent instrument. It is less reliable for unfiltered than for filtered radiation. At present I am unwilling to place sole reliance on these instruments. I use such instruments daily, but I depend largely on carefully interpreted skin effects.

Dr. William H. Guy, Pittsburgh: This paper is one in which the potentialities are more serious perhaps than is realized, because the lay public, particularly the legal end, is watching professional views on radiodermatitis, and the number of suits each year becomes greater. Further, it is difficult to obtain insurance covering x-ray burns. Those individuals who are operating are subjected to the closest scrutiny before insurance companies will take the risk. One point I think should be emphasized in regard to dosage, size of application and so on, which is of the utmost importance in estimating the proper dosage in a given case, and that is the varying susceptibility of individuals. This is a moot point, but I am convinced that such a susceptibility does exist among patients, irrespective of dry blond skins or oily skins, and that it is a fact that patients often react to a dose that is well under an erythema dose. I have compared a few such patients with a normal individual of known susceptibility. I accomplish this by taking the arm of a known type and laying it beside that of the unknown type, applying the same dose of rays and noting the reaction that occurs. I found in a small series of patients that a certain proportion do have a definite susceptibility to roentgen rays. An objection may be made to this, that the manner of living, the amount of cosmetics and soap patients use, and the varying conditions in daily life may well determine differences in reactive phenomena; but these differences apply in all therapeutics and certainly do not argue against the essential fact that patients vary in the degree of reaction to the application of radiant energy.

Dr. C. Guy Lane, Boston: During the past twelve years I have had an opportunity to see most of the dermatologic cases in which the patients have been referred for therapy in the x-ray room at the Massachusetts General Hospital. In this department the interns change every three or four months. They are trained in roentgen therapy but have not had previous superficial therapy. Occasionally an assistant roentgenologist has been there for a period of time and has become competent to go ahead with the dermatologic therapy. It may be interesting to outline the method of educating these men. Emphasis is placed on the choice of diseases to be treated and the stage; the type of patient who should be treated, in respect to age, coloration, and the like; the necessity for definite standardization of apparatus, particularly the amount of previous treatment, both roentgen therapy and other recent therapy; the question of size of the area that is to be treated; the effect of the summation of doses, in that any previous roentgen therapy should be considered in estimating the doses to be given, and the necessity of examining areas that are not then under treatment. In addition, on the record there is a special column devoted to the total amount of treatment in skin units, and that is added to, so that the physician always has before him the total amount of treatment the patient has received at the institution and that is combined, so far as ascertainable, with the amount the patient has received elsewhere. By continually stressing these facts, we have attempted to improve results and to impress on these men the need for the utmost care in the therapy of dermatologic conditions.

Dr. George M. MacKee, New York: Dr. Hazen mentioned the delayed appearance of telangiectasia. I do see remarkably delayed cases. I think that the vast majority appear within two years, but I had one patient in whom a mild telangiectasia developed fifteen years after a single mild erythema dose. Apparently, the condition may appear any time from six months to twelve or fifteen years. The later it appears, the less severe it is likely to be. Also, in many instances, telangiectasia tends to become less marked with the passage of time. This is especially true of the very severe cases. Dr. Hazen mentioned filtration as a safety factor. I agree that there is a little more safety with filtered radiation than with unfiltered radiation, but on the other hand the deep effects of filtered radiation may, at times, be injurious. I am still in doubt whether a thin filter (0.5 mm. of albuminum) should be used as a routine or whether to adhere to unfiltered radiation. Possibly, in the future it will be necessary to use filtration because of greater accuracy when dosage is estimated with instruments such as modern practical ionization dosimeters calibrated in the international x-ray unit known as the roentgen. I agree that the best treatment for a third degree ulcer is excision or plastic surgery. Treatment of sequelae must be selected for the individual case. So-called x-ray skin that frequently ulcerates or in which keratoses are constantly developing should be removed by plastic surgery. In the literature, stress is placed on the total dosage. One wants to know that, of course, but more information is required. One wants to know not only the amount but how it was given: the intervals between treatments—one-fourth unit, for instance, given once a week or one unit given every three or four weeks. Dr. Hazen mentioned the combined effect of irradiation and various topical applications. I agree that ointments containing fairly large amounts of irritating chemicals lessen the toleration of the skin for x-rays or radium, and I believe that such applications should be avoided when radium or x-rays are being used. Erythema or exfoliation evoked by topical applications may hide x-ray erythema, and this may be one reason why telangiectasia is thought by many to occur in the absence of antecedent x-ray or radium erythema.

Dr. Howard J. Parkhurst, Toledo, Ohio: The undesirable sequelae are most likely to ensue in conditions which tend to recur or persist, such as sycosis vulgaris, recurrent dermatophytosis, recurrent or generalized neurodermatitis, and especially the generalized type of psoriasis. In many instances it frequently becomes necessary to substitute other forms of treatment. One great danger of undesirable sequelae occurs in irradiation of acne by overlapping on the anterior portion of the neck, as one cheek is treated and then the other. Another condition in which danger lies is the stubborn nail disease, particularly psoriasis of the nails, which may be irradiated for some time without appreciable benefit.

Dr. Thomas W. Murrell, Richmond, Va.: I believe that many men think they are covered by insurance when they are not. I called up my insurance agent and asked, "Am I covered for radium and x-ray dermatitis in my group insurance," and he told me that I was. I asked him to look it up that I might be sure. He called back and said that he thought I was, so I asked him to write the main office of the company and find out definitely. He told me later that the company said I was not covered, but that I could be if I paid an additional fee. I paid that promptly. This is just an example of an insurance company that has been in business in Richmond for fifty years thinking I was covered by my group policy, when I was not. I think it is advisable in all instances to find out from one's company directly whether one is covered or not before a suit comes up.

Dr. Samuel Ayres, Jr., Los Angeles: Another point that might be mentioned is the occurrence of roentgen sequelae following the use of carbon dioxide snow on areas that have been previously irradiated. I am not sure that we dermatologists

always inquire into the possibility of previous roentgen treatment when we contemplate using carbon dioxide snow. I recall one instance in which carbon dioxide snow was applied for about thirty seconds with firm pressure in a patient who had received irradiation several months previously without any harmful x-ray effects. Following the application of snow, an ulcer the exact size and shape of the snow pencil developed, which took about two months to heal.

DR. H. H. HAZEN, Washington, D. C.: I wish to mention the danger of patients having roentgenograms taken by dentists. I think that the taking of an unrestricted number of dental pictures in a patient who has had quite a good deal of treatment for acne, for instance, is very dangerous. A second point is that too many roentgenologists are inclined to treat patients without finding out definitely how much treatment they have already received. One should be extremely cautious about finding out all the details of previous therapy.

Clinical Notes, Suggestions and New Instruments

ALLERGIC MANIFESTATION TO INSULIN

WILLIAM H. GRISHAW, M.D., LOS ANGELES

A study of this case was undertaken because of the marked allergic manifestations to certain insulin products and because of the therapeutic problem which it presents.

C. G., a man, aged 38, gave a history of bilateral pleurisy at the age of 16, which was diagnosed as tuberculosis and treated with rest for a period of about two years. He had had influenza while in the army in 1918, with a recurrence of the old chest condition, and pneumonia in 1922. For many years he had experienced attacks manifested by a rash over the body, with swelling of the hands and lips, and itching of the skin, without known cause. The attacks lasted from one to four hours and disappeared spontaneously. His mother had had diabetes mellitus and died at the age of 72. His father died of emphysema. One brother died of asthma.

The start of the present illness was in October, 1929, with a bronchitis. The patient was first seen by me in April, 1930, at which time he complained of thirst, polyuria, and loss of weight of four months' duration. The blood sugar (fasting) at that time was 365 mg. per hundred cubic centimeters of blood, and a twenty-four hour urine specimen showed 3.3 per cent sugar. A diagnosis of bilateral pulmonary tuberculosis with cavitation on the right had been made, and right pneumothorax had been instituted.

The patient was placed on a restricted diet, and with insulin the diabetes soon came under control. With each injection of insulin there appeared a reaction of the skin, with redness, swelling and itching, localized to the site of injection. This local reaction recurred with each injection for the next twenty-five days. On the twenty-fifth day, the day following his sixth pneumothorax, about fifteen minutes after his morning dose of insulin a generalized urticarial eruption with itching developed which lasted about four hours. The evening dose was given from a different bottle of insulin manufactured by the same company, following which he had the same reaction, with additional swelling of the hands, lips and eyelids. The next morning a small test dose from still another sample made by the same company (company A) was given, with a reaction identical to that given the night previous.

Later in the day, after all symptoms and signs had disappeared, a similar dose of insulin made by another firm (company B) was given and was followed in ten minutes by urticaria, itching and edema. A trial dose from still another firm (company C) gave no reaction whatever, and the patient has continued using this firm's insulin for the past twelve months, with no local or general reaction.

Insulin specimens taken at random, manufactured by these firms and including the specimens to which he originally gave general reactions, were used for intradermal tests, with the result that all insulin specimens manufactured by company A and company B gave definitely positive reactions, while those of company C gave negative results. Company A supplied me with insulin from both pork and beef pancreas as a source and also a "Special" U-80 preparation. These specimens gave positive skin tests. From company B I obtained their end-product in powdered form and a "purified" insulin also in powdered form. These powdered specimens were made up to U-40 strength, hundredth normal hydrochloric acid being used as a solvent, and the reaction was then adjusted to p_H 2.5. The stock powdered product gave a positive skin reaction while the "purified" gave a negative test. Beef, pork and veal proteins all gave negative skin reactions. The specimens to which the patient reacted have been tried intradermally in other patients with diabetes mellitus and no reaction was observed.

In order to determine whether the substance to which he reacted could be precipitated, various concentrations of acetone were added to the insulin specimens, and after filtration the acetone was driven off. The acetone-free filtrates of the specimens to which he reacted, tested intradermally, all gave negative tests. Both the insulin specimens and the filtrates have been tested intradermally on various occasions during the past year and the patient gave identical reactions at all times.

Presumably a part or all of the insulin activity was removed by the precipitation, but in order to determine whether there was any insulin left in the filtrates I injected mice with insulin to establish a control, and then with the filtrates. The mice were divided into four groups of three males and two females to the group. The first group received $\frac{1}{150}$ unit of insulin per gram of body weight; the second, $\frac{1}{125}$ unit per gram; the third, $\frac{1}{100}$ unit per gram, and the fourth, $\frac{1}{75}$ unit per gram. The result was an increasing number of convulsions over a given period of time with the increase in dosage. This was repeated, the filtrate being used in the same dose for the various groups, and the dose of the filtrate then being increased to ten times the original. With the filtrate there was no demonstrable effect on the animals.

Results of Tests with Insulin from Various Manufacturers

Firm	Insulin	Source	Skin Reaction	Acetone Free Filtrate Reaction
Co. A	U-80	Pork	Positive	Negative
	U-40	Pork	Positive	Negative
	U-40	Beef	Positive	Negative
	U-80	"Special"	Positive	Negative
Co. B	U-80	Beef	Positive	Negative
	U-40	Beef	Positive	Negative
	U-40 (powdered end-product)	Beef	Positive	Negative
	U-40 (purified powdered)	Beef	Negative	Negative
Co. C	U-40*	Beef	Negative	Negative
	Proteins			
	Beef		Negative	
	Pork		Negative	
	Veal		Negative	

* This product he is now using.

Dr. R. W. Lamson offered to attempt passive transfer skin tests on a small group of patients in the allergy clinic. This was done by sensitizing the skin with a 1 to 1 dilution of the patient's blood serum and twenty-four hours later injecting the insulin and filtrate intradermally, physiologic solution of sodium chloride being used as a control. No positive skin tests were obtained by this method. In other words, Dr. Lamson was unable to transfer passively this patient's sensitivity.

COMMENT

This patient reacts to insulin manufactured by two firms but not to that of a third firm, which indicates that he is not sensitive to insulin, as was at first thought, but is sensitive to some substance contained in the product of companies A and B but not in that of company C. This substance is precipitable and gives reactions similar to those seen in individuals sensitive to protein and to pollen.

1930 Wilshire Boulevard.

Council on Pharmacy and Chemistry

INTRAVENOUS USE OF BARBITAL COMPOUNDS

The Council has authorized publication of this report on the intravenous administration of barbital compounds.

W. A. PUCKNER, Secretary.

More than seven years has elapsed since the introduction of the intravenous use of barbitals, sufficient time to justify an assay of the possible value of the method. The chief object of intravenous use has seemed to be the possible employment of barbitals used in this way to produce anesthesia. All the possible changes following intravenous injection, a comparison of the experimental and clinical results, and a determination as to whether the intravenous use has peculiar advantages over other methods of administration, with equal safety, are here considered. There is no doubt that the characteristic hypnotic action of the barbitals can be obtained by oral administration. Since the barbitals act essentially as hypnotics, and not as anesthetics, it is reasonable to entertain doubts about radical departures from the orthodox usage of these drugs. Nevertheless, new methods of using and new uses for well known drugs merit attention. Moreover, the intravenous use of barbitals has been widely exploited by some manufacturers and serious attention has been given to the subject experimentally and clinically. The following considerations are based on an examination of the literature on intravenous medication as it concerns the barbitals.

HISTORY

The clinical use of barbitals intravenously dates from Fredet and Perlis[1] in France, who tried diethylallyl barbituric acid (somnifene) in 1924. Three years later, in 1927, secondary butylbromopropenyl barbituric acid (pernocton) was used in a similar way by Bumm[2] in Germany. Following the experimental trial of sodium isoamylethyl barbiturate by Page and Coryllos[3] in 1926, in this country, there came a period of intensive exploitation of this barbital derivative intravenously beginning with a preliminary report by Zerfas, McCallum, Shonle, Swanson, Scott and Clowes[4] and a clinical report by Zerfas and McCallum,[5] both in 1929. During the next two years several reports on experimental studies in animals appeared. However, by the year 1931 the reports on amytal and other barbitals intravenously decreased appreciably in number. There was likewise a decline in enthusiasm over the method. In fact, by 1931 most clinical reports that showed evidences of effort to determine the value of these drugs for intravenous anesthesia concluded that all the actions and benefits from the barbitals were obtainable from oral administration, as well as, if not better than, from intravenous administration. This moderation in claims for intravenous use by physicians coincided with a cessation of intensive exploitation by manufacturers.

1. Fredet, P., and Perlis, Régine: Bull. et mém. Soc. nat. de chir. **50**: 789, 1924. Perlis, Régine: Presse méd. **32**: 675 (Aug. 13) 1924. Clin. and Perlis: Ibid. **32**: 18, 1924. Fredet, M.: Ibid. **33**: 288, 1925.
2. Bumm, R.: Klin. Wchnschr. **6**: 725 (April 16) 1927.
3. Page, I. H., and Coryllos, Pol: J. Pharmacol. & Exper. Therap. **27**: 189 (April) 1926.
4. Zerfas, L. G.; McCallum, J. T. C.; Shonle, H. A.; Swanson, E. E.; Scott, J. P., and Clowes, G. H. A.: Proc. Soc. Exper. Biol. & Med. **26**: 399 (Feb.) 1929.
5. Zerfas, L. G., and McCallum, J. T. C.: J. Indiana M. A. **22**: 47 (Feb.) 1929; Anesth. & Analg. **8**: 349 (Nov.-Dec.) 1929.

The barbitals will not be considered individually in this report; a collective summary will suffice. Probably the most extensive, and likewise most reliable, studies have been made with amytal. Incidentally, it may be questioned whether wholesale clinical experimentation with a drug whose actions could have been predicted from results on animals was necessary or desirable. It is now generally conceded that all the barbitals act alike qualitatively, differing only quantitatively, so that nothing is to be hoped for in the way of better and safer therapeutics from a barbital alleged to be effective in small dosage. The old law of pharmacology which teaches that efficiency varies directly with toxicity has not been invalidated among the various barbitals placed before the medical profession. Nor are the chemical and physical properties of the barbitals sufficiently different in material ways to influence the present consideration.

EFFECTS ON THE BLOOD

In considering the effects of intravenous use of barbitals, both the direct effects on the blood of the injected barbitals, and reflex or remote effects caused within the circulatory system—secondary effects not aimed at or necessarily desired in their use as hypnotics and anesthetics—must be kept in mind. The barbitals are insoluble organic acids which require large amounts of alkali for solution. Amytal, for instance, requires a degree of alkalinity the equivalent of a buffer solution with p_H 9.5 or 9.8, or the reaction of nearly a ten thousandth normal solution of sodium hydroxide, which is approximately 900 times as alkaline as the blood (p_H 7.2 to 7.4). Solutions of sodium amytal with p_H 9.2 to 9.3 give incomplete and imperfect anesthesia with disturbing effects. Amytal, and for that matter any other barbital, will not remain in solution with the chemical reaction of blood, but is precipitated. Therefore, after intravenous injection, the barbitals must be precipitated in the blood stream or exist in a finely divided physical state, possibly adherent to the formed elements and the proteins of the blood. The situation then is the presence of a foreign body in the colloidal state within a sensitive colloidal system, namely, the blood, whose physical-chemical properties and physiologic function are unintentionally and undesirably affected. There is certainly no evidence in favor of a beneficial action on the respiratory function of the blood under these conditions and no reason for believing that such an action occurs. On the contrary, the changes produced by such foreign bodies, with extensive surfaces, are generally undesirable and harmful. The actions just mentioned have been adequately demonstrated for a large variety of agents by many authorities.[6]

The changes resulting from the disturbed colloidal state of the blood are quite independent of the intrinsic pharmacologic actions of the barbitals. These changes occur with all barbitals, but the weaker the barbital happens to be, pharmacologically and toxicologically, the greater will be the mass of the precipitate in the blood. Since the extent of tissues and blood surfaces involved is probably proportional to the mass of precipitate, and the immediate or colloidal disturbances depend on some surface action mediated by the flocculated material, the physiologic changes, including reflex reactions, may be out of proportion to the intrinsic toxicity. An exact correlation of the physical changes and the functional reactions is not possible,

6. Hanzlik, P. J.: The Basis of Allergic Phenomena, J. A. M. A. **82**: 2001 (June 21) 1924.

but it can be seen that the physical state in which a barbital exists in the blood stream may modify the true pharmacologic action and contribute to or determine a greater toxicity. In any case, the net result of introducing such a foreign body into the blood cannot be regarded except as objectionable and potentially dangerous. This aspect of the intravenous use of barbitals has been generally overlooked in considering the toxicity and activity of these drugs, although they have been generally regarded as giving variable and irregular results. Probably the explanation of the irregularities lies in the complicated changes arising from the physical properties of the barbital solutions and the disturbed colloidal state of the blood.

A concrete illustration of complications accompanying intravenous injections is an important group of reflex actions, which may be mentioned here, since these might arise from the disturbed colloidal equilibrium of the blood, or from marked alkalinity of the injected barbital solution, or both. These may be referred to as the intravenous reflexes, invoked as the result of irritation of the depressor nerve endings in the base of the aorta and heart, of the vagus nerve terminations in the viscera, but especially the heart and lungs, and of the carotid sinuses. The changes would be manifested by sudden circulatory and respiratory disturbances, such as a fall of blood pressure, slowing or acceleration of the heart, and generally acceleration of the respiration. Again it is not necessary to present here the evidence for these changes, which have been well demonstrated by many investigators, especially by Heymans and his co-workers,[7] who have used alkaline solutions, alkaloids, irritants and other agents. The invocation of intravenous reflexes, real or potential, by the injection of barbitals into the blood stream adds unnecessary and undesirable complications to the ordinary hypnotic action of these drugs and to their use as aids in anesthesia, both systemic and local. However, these immediate reactions do not represent the direct protoplasmic or intrinsic pharmacologic actions which are manifested by many functional and tissue changes occurring independently of, or concurrently with, the reflex actions. The two cannot be easily separated. The following lists of the actions and their mechanisms, observed experimentally and clinically, should serve to emphasize the complex nature of the profound effects caused by the barbitals intravenously.

EXPERIMENTAL PHARMACOLOGIC EFFECTS

Experimentally,[8] the intravenous use of nonfatal, though definitely effective, doses, such as from 25 to 40 mg. per kilogram of body weight, of sodium amytal advocated for anesthesia causes:

1. An immediate and sustained fall of blood pressure, the degree and duration of which is determined by the dosage, the rate of injection, and the nature of solution used.
2. Acceleration of the heart and paralysis of the vagus nerve control of the heart (except possibly phenobarbital) lasting from a few minutes to three hours, presumably due to ganglionic depression, since pilocarpine and choline still give their typical cardiac slowing.
3. Cardiac depression.
4. Depression of gastric and intestinal motility, flaccidity of the stomach and decrease in intestinal absorption of sugar.
5. Depression of smooth muscles of the intestine, uterus and blood vessels.
6. Reduction in the consumption power of skeletal muscles for sugar.
7. Hyperglycemia, with or without glycosuria.
8. Respiratory depression and irregularity.
9. Rapid fall of body temperature (about 2 to 3 degrees C.) lasting from one to three hours with shivering and increase in basal metabolism followed by a decrease of from 4 to 13 per cent.
10. Prolonged narcosis accompanied by lively reflexes and considerable, though variable, restlessness, tremors and twitching.
11. Cerebral ischemia with cortical excitability preserved.
12. Depression of basal ganglions in the brain.
13. Decreased or increased urine output presumably varying with the degree of circulatory depression.
14. Decreased excretion of phenolsulphonphthalein.
15. Decrease in diuresis of thyroxine.

Most of the acute effects occur from three to four minutes after injection. Higher doses have caused depression of the spinal cord and peripheral nerves with loss of reflexes, vasomotor paralysis, circulatory collapse, marked respiratory depression and deep coma, capillary paralysis (arsenic-like), mucoid degeneration of the brain, and not uncommonly sudden death. Barbital is the least and amytal and pernocton are the most toxic for the circulation. Selective distribution of all barbitals to the thalamic region of the brain is

7. Heymans, Corneille: Le sinus carotidien, Brussels, Revue belge des Sciences médicales, 1929, p. 121.

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reported. Excretion of barbitals is comparatively slow, lasting about a week, the drugs tending to accumulate without complete destruction, except possibly amytal. Coma is lasting but may be accompanied by restlessness and tremors until death. Recovery from anesthetic doses is variable but may require up to thirty-six hours.

Most of these actions have also been demonstrated after gastric and hypodermic administrations, except that the actions are slower and the initial fall of blood pressure does not occur and the later fall is not precipitous. This means that the gastro-intestinal and tissue absorption of the barbitals is definite and reliable, from which it follows that all the desired actions can be obtained by giving these drugs by mouth, and that the sudden undesirable actions on the blood and the collapse can be avoided, and, in fact, the sedative and hypnotic actions more satisfactorily controlled.

The toxic and fatal doses of the different barbitals have been found to vary considerably with the chemical grouping in the barbituric molecule, but the activity has varied in the same direction. In no case has the margin of safety been increased by increasing the general activity. Moreover, and this is important in the use of barbitals intravenously for a high degree of depression or for anesthesia, most investigators agree that the margin between doses giving such severe actions and the fatal dosage is too narrow for safety. In dogs, the average oral, rectal and intravenous anesthetic doses of amytal are reported to be about 55 per cent of the minimum fatal dose, but considerable variability exists. Anesthesia may not occur with doses becoming fatal.

In the treatment of the toxic and collapse actions, caffeine, epinephrine and ephedrine, used individually or combined, intravenous dextrose solution, and picrotoxin have been tried with variable success, generally with temporary benefit in frank collapse and with better results during impending, suspected or partial collapse, or if used as prophylactics; but the treated animals under these conditions might have recovered without the use of these antidotes.

CLINICAL STUDIES OF BARBITALS GIVEN INTRAVENOUSLY

Clinically,[9] the following actions after intravenous injection of barbitals, chiefly sodium amytal, have been reported:

1. Full effectiveness of from 12 to 25 mg. per kilogram in from three to five minutes.
2. Difficulty in determining exact and desired dosage.
3. Immediate and sometimes precipitous fall of blood pressure, from about 15 to 30 mm. and up to from 40 to 60 mm. of mercury, according to the dose, rate of injection, physical character of the solution and original level of blood pressure.
4. Slowed, shallow and irregular respiration.
5. Increased pulse rate.
6. Unconsciousness.
7. Deep sleep.
8. Cyanosis.
9. Preservation of reflex activity.
10. Laryngospasm.
11. Severe coughing.
12. Muscular rigidity.
13. Incomplete and imperfect analgesia.
14. Depression out of proportion to toxicity.
15. Retention of mucus in respiratory passages.
16. Decreased urinary elimination, urine containing trace of acetone.
17. Increase in phenolsulphonphthalein excretion at first, decrease later.
18. Transient renal irritation.
19. Decrease in oxygen consumption and tactile discrimination.
20. Allergic reactions with amytal and phanodorn.

Man is more sensitive than are animals. Mild euphoria without sleep and narcosis occurs after 60 mg. of sodium amytal.

In obstetrics, the second stage of labor and uterine contractions are not usually changed, but the infants are frequently apneic and require respiratory stimulation. Excretion of phenobarbital in milk is reported.

Postoperative actions have been reported as follows:

1. Prolonged depression lasting from twelve to eighteen and up to thirty-six hours, according to the dose and the individual.
2. Lack of patient's cooperation and orientation, and considerable confusion.
3. Restlessness and delirium, swallowing of tongue and cyanosis.
4. Decrease in intake of fluid and voiding.
5. Pulmonary congestion and edema due to shallow respiration.
6. All actions profound in the aged and debilitated.
7. Sudden awakening during operation under local anesthesia.

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Caffeine and ephedrine have been tried in treating toxic symptoms and collapse, but with variable success, and most surgeons concede the inadequacy of reliable antidotes. All these actions generally agree with those observed experimentally in animals, although it is unfortunate that a clean-cut comparison is not possible in the case of amytal, since the patients in most of the clinical reports received additional medication with morphine, scopolamine or atropine, or combinations of these drugs.

The following clinical uses of the barbitals (somnifene, pernocton, but mainly amytal), intravenously, have been recorded:[9]

1. Intravenous anesthesia, without success, however, because complete analgesia cannot be obtained and volatile anesthetics must be supplemented.

2. Preanesthetic medication for allaying nervousness, fear, apprehension and excitation before operation.

3. For smoother systemic anesthesia, for decreasing the amount of volatile anesthetic and for increasing the concentration of oxygen (up to 30 per cent) in gas anesthesia.

4. Control of convulsions of tetanus, strychnine, epilepsy and eclampsia.

5. Prevention of excitation and convulsions of local anesthetics in overdosage, or in susceptible patients, and of excitation of delirium tremens and narcotic addiction.

6. Elimination of fright and apprehension of patients with exophthalmic goiter before operation.

7. Control of postoperative psychosis, persistent hiccup, generalized pruritus, and postoperative convulsions of craniotomy and cranial injuries.

8. Occasional intense pain of broken back, extensive burns and gastric crisis unrelieved by morphine.

9. In operative and diagnostic procedures of upper air passages.

10. Preparation for local anesthesia.

These uses would be indicated from the general pharmacologic actions of the barbitals and would be met for the most part, except in rare emergencies, by oral or hypodermic administration.

The clinical advantages claimed for the intravenous use of barbitals, chiefly according to experiences with amytal, are:[9]

As preanesthetic medication:

(*a*) There is normal induction of sleep without struggling; gradation of action is more speedily achieved.
(*b*) Operation can be begun sooner.
(*c*) It permits smoother systemic anesthesia, procures calm, and eliminates undesirable effects of excitation of local anesthetics and shock.
(*d*) All preparation of the patient as to position on the table and cleansing and draping of the operative area can be done just before inhalation anesthesia.
(*e*) Abdominal operations can be performed with gas anesthesia but without local anesthetics.
(*f*) It is comfortable to the operator.
(*g*) It reduces the amount of volatile anesthetic and permits the use of a higher concentration (from 16 to 32 per cent) of oxygen, thus eliminating asphyxia and the like.
(*h*) The range of operation is extended.
(*i*) Operation is more of an artistic achievement.

Postoperatively the barbitals, it has been claimed, give easy, painless recovery; eliminate nausea and vomiting; leave memory free from disagreeable impressions; reduce need for morphine except in case of delirium, excitation and restlessness; and give rapid action in control of convulsions of toxic or disease origin. It is claimed that barbitals are more nearly suited to intravenous injection than other acids and hypnotics, such as chloral and avertin, but they are not necessarily superior to other hypnotics by other routes.

The disadvantages of the intravenous use of the barbitals may be listed as follows:[9]

(*a*) The special preparation and adjustment of solution for injection of barbitals, especially if the sodium salts are not readily available, is inconvenient.
(*b*) Solutions are not always clear.
(*c*) Delays and annoyances accompany the method.
(*d*) Intensive vigilance of the attendants is required.
(*e*) The alkalinity of the solution is greater than that possible in the body, and therefore irritation occurs.
(*f*) There is unnecessary injury to the blood and the danger of colloidal shock.
(*g*) There are unfavorable intravenous reflexes.
(*h*) There is danger of pulmonary embolism.
(*i*) Determination of the exact dosage is difficult.
(*j*) There is the danger of sudden and alarming fall of blood pressure, resulting in collapse, which might postpone or complicate operation.
(*k*) There is marked respiratory depression and irregularity.
(*l*) Reflex excitability is increased.
(*m*) In operations on the upper air passages, poor relaxation of the masseters and laryngospasm occur.
(*n*) Analgesia is seldom, if ever, attained.
(*o*) The desired action is difficult to obtain.
(*p*) Considerable individual variability exists.
(*q*) In case of overdose, the drug cannot be retrieved.
(*r*) Proposed antidotes are not dependable or satisfactory.
(*s*) The duration of action is too brief for satisfactory operations.
(*t*) Without the usual preanesthetic aids, such as morphine and scopolamine, and supplementary anesthesia with volatile anesthetics, barbitals cannot be relied on for use in operations.
(*u*) Useful cooperation and sudden awakening of the patient operated on under local anesthesia are eliminated.
(*v*) In surgery, the field of usefulness is narrow and limited.

In obstetrics:

(*a*) There is the danger of asphyxiation of the child and restlessness of the mother.
(*b*) There is undesirable general protoplasmic poisoning.
(*c*) The postoperative depression is prolonged, the anesthetic state continuing and resulting in lack of the patient's cooperation.
(*d*) There is danger of pulmonary congestion and edema.
(*e*) It is difficult to keep the respiratory passages free from accumulating mucus.
(*f*) Delirium and restlessness may require additional morphine.
(*g*) Intake of fluids is impaired and voiding is omitted.
(*h*) Special postoperative nursing care is indispensable.
(*i*) Occasional toxic dermatitis occurs.
(*j*) The method is contraindicated in aged and debilitated patients.
(*k*) Sudden death may occur

SUMMARY

Except for the more difficult determination and gradation of dosage and the exactness and special care in preparation of a solution of the drug, the sudden blood, reflex and collapse phenomena, and the intensive preoperative and postoperative vigilance over the patient, practically all the disadvantages cited would occur also with administrations other than the intravenous. In other words, any advantages that may exist in the choice of barbitals as aids in anesthesia, or as sedatives, analgesics or hypnotics, can be easily procured by giving them by mouth, with the further advantage of avoiding the necessity of the small operation and aseptic technic for an intravenous injection and the unnecessary disturbances and complications of such injections in general. About the only argument in favor of the

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SATURDAY, DECEMBER 19, 1931

CHEMISTRY'S NEXT SERVICE TO MEDICINE

More than a century ago Laënnec, writing in the first volume of the *Archives générales de médecine*,[1] remarked that the aim of medicine is the cure of disease. For the attainment of this end Laënnec singled out three pathways, described by Cohn[2] as (1) that of the empiricists, who considered it sufficient to distinguish diseases by their apparent signs, (2) that of those who believed it possible to disclose the causes of disease without giving themselves the trouble of learning their effects, and (3) that of those who believed it was necessary to understand the diseases. Cohn adds, by way of interpreting or perhaps of supplementing Laënnec's meaning, that we believe it necessary as the basis of therapeutics to understand the mechanisms, that is to say, the processes which underlie the manifestations of disease, for it is these which it is one of our functions to attempt to correct. That is our practical aim.

For a long time investigators in the domain of the medical sciences have been so deeply engrossed with the efforts to classify diseases and to discover their etiology that practical therapeutics has received somewhat niggardly attention in many quarters. Medical practice has passed through a stage of therapeutic nihilism of which some signs still remain. Obviously, rational therapy depends on the knowledge secured by the intensive study of disease as such; but the relief of suffering and the temporary or permanent correction of defects are inevitable functions of the devotees of medicine. It is not always enough today merely to attempt to reinforce the patient's natural means of defense. The armamentarium of the open minded physician includes for therapeutic purposes drugs, foods, water, serums, vaccines, electricity, heat and cold, mechanical agents, rest, exercise, massage, climate, mental influences and, in fact, whatever physical, chemical and psychic agencies seem to be helpful. To the extent that he may be indifferent to most of these helps he is liable to deprive his patients of some real advantage in the attack on disease.

Students of medicine are sometimes resentful of what they regard as the intrusion of other disciplines or workers in other fields into their domain. This view has been expressed by Cohn in the assertion that a dependence on the outside world for the solution of its problems is in part a reproach to medicine. Probably no injury has yet been suffered, he adds, by society as a result of this dependence. But those advances which depend on knowledge of disease in patients and on actual direct contact with diseased persons have been made by the practitioners of medicine themselves. In this way is to be explained the significance of Sydenham, Jenner and Laënnec; they have taught the use of the classification of diseases, the fact that fevers are preventable, an approach to the diagnosis of visceral disease by means not immediately obvious. These have, after all, constituted the primary advances in medicine. It is this experience which encourages the belief, Cohn concludes, that the development of medicine is in all probability the work of physicians properly trained and supplied with adequate equipment.

In view of the foregoing, it might come as an unpleasant surprise to one not thoroughly conversant with the facts of medical progress to read the title of an essay recently addressed to a group of chemical engineers. The caption was Chemistry's Next Service to Medicine. This contribution, by A. W. Rowe[3] of the Evans Memorial in Boston, deals with the indispensable rôle of the chemist in the preparation of hormones, those substances which are potent regulators of various important bodily functions, such as growth, development, nutrition and reproduction. From drugs to hormones is a relatively simple step. In its pride of accomplishment, medicine must bear in mind that the formal exact study of the action of drugs did not begin until within the lifetime of some living physicians. The first laboratory for the investigation of drugs was established at Dorpat in 1856. Yet chemists had extracted the alkaloid morphine from opium in 1817. Endocrinology, divested of much of its ignorance, misinformation and pretense, seems destined to be one of the major factors in medical progress in the days ahead. The contributions of the chemists in making replacement therapy possible when, as often happens, underproduction of certain hormones leads to the serious effects of endocrine disorder—to serious and even fatal changes in "function level"—deserve frank recognition. Rowe has recalled, for instance, that with their powerful influence on the basic functions of protoplasm any abnormal secretory activity of the individual gland leads to an abnormal expression of those functions over which it exercises a regulating power. End-results such as gigantism, dwarfism,

1. Laënnec, R. T. H.: Arch. gén. de méd. **1**: 5, 1823.
2. Cohn, A. E.: Medicine, Science and Art, Chicago, University of Chicago Press, 1931.
3. Rowe, A. W.: Chemistry's Next Service to Medicine, Indust. & Engin. Chem. **23**: 1176 (Oct.) 1931.

extreme obesity and emaciation, infertility, marked changes in mentality and in the secondary characteristics of sex, and a wide variety of other striking manifestations are thus produced.

The preparation of therapeutically available products representing "active principles" of endocrine tissues has been the contribution of the chemical laboratory. The hormones themselves are only a small part of the individual glandular masses or secretions. Isolation of the potent from the extraneous constituents has often involved great difficulty. Success in the chemical identification of the active components paves the way for chemical synthesis whereby freedom is won from dependence on animal sources often difficult to control. This again is a chemist's job. Rowe has presented challenges to the chemist engaged in this field. The first major problem, he points out, is in the isolation of active extracts, and this has been by no means a simple one. Some of the compounds, at least, are highly labile products and may be destroyed during the processes of extraction by the chemical agents used or even by other materials produced in other portions of the same gland from which they are derived. That insulin, the active material from the islands of Langerhans, a part of the pancreas, is destroyed by the digestive enzymes produced by other cells of the same gland is an illustration of the latter condition. A second problem of moment lies in the standardization of these active principles so that the dose administered may be estimated with some degree of precision. Existing in the organism, as they do, in small quantities and in concentrations capable of producing profound physiologic response, it is essential that means be devised to assay their potency. Even today, many preparations are given on the basis of so many grains or milligrams of the fresh or dried substance without any index of the real content of active material.

A further challenge to the chemist lies in the need of reducing the costs of products now attained through expensive processes of manufacture from unabundant materials. This has an economic rather than a purely scientific import; it is none the less important in the day's work of the physician. Rowe points out that the recently prepared extract from the suprarenal cortex, which has been demonstrated to be effective in Addison's disease, costs about $3,000 a year for the amount necessary to treat a single case. Even in those glandular failures in which the replacement therapy is at a minimum cost level through reasonably large supply of raw material and efficient methods of preparation, it can easily reach $100 a year, a far from negligible sum for a large group of wage earners. Epinephrine and thyroxine can now be produced synthetically. Further progress of this sort will represent contributions the importance of which scarcely needs debate. Rowe further says that adequate amounts of pure standardized chemical entities of established quantitative physiologic activity at reasonable cost will enable physicians to produce an enormous alleviation of human suffering, prolong life, and maintain physical efficiency. Let us not discourage what seems to some as an "intrusion" of the chemist into the domain of medicine.

THE TONSILS IN YOUNG WOMEN

Numerous comments in THE JOURNAL on the need for comprehensive statistical studies on the results of tonsillectomy, particularly in relationship to the important investigations made by Kaiser,[1] have apparently stimulated others to similar studies. Now Cunningham, at the University of California, has studied the results of the physical examination of 14,000 women students during the last ten years. More than a third of the young women entering the university during that period had a tonsillectomy; another third were considered as having normal tonsils; the tonsils in the remaining third were considered pathologic. The study was confined to white women students under 35 years of age, as well as to those concerning whose medical history important information could be obtained. The physical examinations required of all entering students were made mostly by specialists, three of whom served during the entire ten years. While the accuracy of the original histories may have suffered as a result of the haste and excitement attending the entrance examinations, the physical examinations were probably fully as accurate as records of the examinations for the army.

In her study of this work, Cunningham[2] endeavors to bring out the relation of the condition of the tonsils to the infectious diseases of childhood. Especial attention was given to cardiac conditions, for the results of these examinations determine where the student is placed in physical education classes in the university. Evidence of damage to the mitral valve was less among those with normal tonsils than among those students whose tonsils were absent or pathologic; in this respect the latter two groups seemed to suffer equally. The group whose tonsils had been removed showed about half the percentage of damage of the aortic valve that was shown by the group whose tonsils were thought to be normal and about one third of the percentage of damage of those whose tonsils were considered pathologic. Of course, tonsillectomy will not guarantee a halt in the progress of existing cardiac disease, and if the operation is to be used as a therapeutic measure it will produce the best results when done before the cardiac infection occurs or early in its course. The two groups of students with normal and with pathologic tonsils had about an equal number of painful experiences, which in

1. Kaiser, A. D.: Effect of Tonsillectomy on General Health in Five Thousand Children, J. A. M. A. **78**:1869 (June 17) 1922; Effect of Tonsillectomy on the General Health of Twelve Hundred Children as Compared with an Equal Number Not Operated on, ibid. **83**:33 (July 5) 1924; Results of Tonsillectomy, ibid. **93**:837 (Sept. 20) 1930; The Relations of Tonsils and Adenoids to Infections in Children, Am. J. Dis. Child. **41**:568 (March) 1931.

2. Cunningham, Ruby L.: Normal, Absent and Pathologic Tonsils in Young Women: A Comparison of Histories, Arch. Int. Med. **47**:513 (April) 1931.

their history may or may not have indicated previous attacks of rheumatism. There was a significant difference, however, between the two groups with normal tonsils and those on whom a tonsillectomy had been done. A high proportion of persons whose tonsils had been removed had had rheumatism.

The medical histories of these students were studied also to learn what relation existed between the tonsils and diseases of the respiratory tract, otitis media and the infectious diseases of childhood. The group with absent tonsils gave a history of a higher incidence of all illness and operations than did either of the other two groups. A possible explanation for this is that children who are often ill were most frequently operated on. The group of women students with normal tonsils and the group with pathologic tonsils differed little in the percentage of the incidence of measles, mumps, scarlet fever, diphtheria, chickenpox, whooping cough, rheumatism, pneumonia, pleurisy, chorea, chronic colds and in operations for appendicitis, mastoiditis, cervical glands and operations on the nose. The age when the tonsils were removed had no influence on the total incidence of measles, mumps, chickenpox, whooping cough, pneumonia and influenza. However, early removal of the tonsils seemed to have a slightly favorable influence on the incidence of scarlet fever and diphtheria.

Considering the large number of tonsillectomies and adenoidectomies that have been performed, it is unfortunate that the literature reveals a great lack of accurate information on the effect of tonsillectomy. Opinions still differ on this old question. There seems to be a growing tendency to question the value of tonsillectomy as a prophylactic measure against infectious diseases and as a cure for rheumatism, chorea and carditis. The report of this study agrees, in general terms, with the report of Collins and Sydenstricker, reviewed [3] in THE JOURNAL in 1928, and also with the studies of Kaiser. It indicates that tonsillectomy is a useful procedure, but the benefits, when a large control group is compared, are not so striking as could be desired.

COOPERATION IN NECROPSY WORK

The percentage of necropsies performed in this country is still lamentably low. A properly performed necropsy is not only necessary in many cases to establish the exact cause of death but is one of the chief means of advancement of medical knowledge. The reasons for failure to obtain necropsies are obvious. The physician in charge of a case lacks the scientific urge, the relatives of the deceased are opposed, and the mortician is, to say the least, cool, because necropsies may disturb the routine of his work. A joint committee of the New York Academy of Medicine, the New York Pathological Society and the Metropolitan Funeral Directors' Association recently held a series of meetings to discuss the problem. A substantial agreement was reached. All agreed that a necropsy by a pathologist is desirable in order to advance knowledge concerning the nature of the disease and to provide reliable records. The performance of necropsies in a hospital is a constant influence to improve the service and to help physicians serve the next patient with greater confidence and skill.

The hospital and its staff have not completed their services to the family on the death of the patient, but they owe to the family an account of what has occurred. This requires that a representative member of the family come to the hospital for a personal interview and to give permission for examination of the body of the deceased. The funeral director must recognize this relationship and should not oppose the discharge of this obligation. Unreasonable delay by the hospital in its attempt to obtain permission for necropsy is objectionable to a funeral director, as it may require him to cancel contracts for transportation and other services and thus increase his expense. The conflict of interests requires mutual consideration and cooperation. Arrangements should be worked out in every hospital whereby the unnecessary loss of time on the part of the funeral director may be obviated. Hospital employees in general must not give information to funeral directors or to any other unauthorized person in regard to persons critically ill or dead in the hospital. The hospital authorities should be certain that the necessary data for a death certificate are on the chart at the time of admission of the patient, with exception of the facts relating to the nature, progress and termination of the disease. Any interference by a funeral director with the legitimate efforts of the hospital to obtain permission for necropsy shall be regarded as a reportable grievance. The necropsy may be performed in a way to facilitate the work of the embalmer. The main longitudinal incision, the committee believes, should end over the midsternum, and curved incisions with the concavity toward the head should be carried laterally to each shoulder. When the skull is opened, the frontal bone should be cut above the hairline and the base of the skull cemented with plaster before the skull cap is replaced. When the neck organs and tongue are removed, the head should be embalmed through the carotids unless there is a serious contraindication. Other recommendations made by the committee as to technic are that necropsies should be completed at the time promised, if there has been an advance agreement, and that a representative of the funeral director should be a welcome associate at the necropsy table. The spirit of cooperation shown in the report of the joint committee is commendable. Similar cooperation everywhere would no doubt result promptly in an increase in the percentage of necropsies.

Gradually, competent embalmers are tending toward the encouragement of postmortem examination. In

3. Tonsillectomy in the United States, editorial, J. A. M. A. **91**: 1195 (Oct. 20) 1928.

the November issue of the *Casket and Sunnyside*, a publication for morticians, appears an editorial commenting on a previous statement on this subject by THE JOURNAL. The concluding statement of this editorial reads:

> We might as well recognize, first as last, that the welfare of the living, the public health, is the chief concern of the public, and that to permit the medical profession to secure sufficient scientific data, autopsies must be performed. We might as well also decide that if we explain our difficulties to the medical practitioners, rather than antagonizing them, they will be willing to cooperate with us in avoiding unnecessary mutilation of bodies committed to them for autopsy. Finally, we might as well realize that if we say "an autopsied body can't be embalmed or so prepared that family and friends may view it," we're stultifying ourselves and our claims to professional standing, and admitting our own incompetence.

The editorial points out further that the mortician should be proud of his ability to make presentable a body that has been subjected to postmortem examination and that the cry against such examinations on the part of morticians must be taken as a confession of incompetence. Such support from one of the leading trade publications in the field is an encouraging sign to scientific medicine. It means that the pathologist will now need only to instruct the family and not to convince the mortician.

MATERNAL MORTALITY

The propaganda which has made most of the people in the United States and elsewhere believe that our maternal mortality is worse than that of any other country in the world is difficult to overcome regardless of its inaccuracy. In his International Studies on the Relation Between the Private and Official Practice of Medicine, Sir Arthur Newsholme [1] has pointed out that international comparisons are not dependable because of the great variation that exists in different countries. In developing such statistics it is possible to discover considerable differences in puerperal death rates which do not correspond with real differences. The practices in England and Scotland do not differ markedly, but those in the Netherlands and in the United States differ greatly from those in England and Scotland. Indeed, Sir Arthur Newsholme feels that the international position is somewhat chaotic and that it is doubtful whether the chaos could be removed by the adoption of a rigid and detailed international system of rules, so much depending on the personal bias of the statistician responsible for relegating a dubious certificate embodying more than one item to its right compartment.

Recently, Dr. Robert J. Lowrie [2] has indicated the serious character of the difficulty of properly evaluating death certificates involving puerperal mortality in this country. Not every death certificate on which there is mention of pregnancy or childbirth can count as a maternal death, because pregnancy and childbirth are frequently complicated by cardiac disease, hyperthyroidism, tuberculosis, syphilis and similar complications. Reports of cases are available in which a fever appearing post partum was associated with the appearance of congestion of the lungs in a patient with a long history of tuberculosis. The question as to whether the fever was due to puerperal sepsis, pneumonia or recurrent manifestations of tuberculosis involved a decision too delicate to be shown adequately on the death certificate. Dr. Lowrie feels that our present method of determining maternal mortality rates is quite inaccurate and he offers a new system which is of interest. The analysis of the technic involved is a matter for biometricians.

Every one should realize the impossibility of accurate comparisons between maternal mortality rates in various countries and, indeed, in individual communities in the same country, in hospitals and in general practice. Enough evidence has been developed to indicate that proper prenatal care and adequate obstetric care will lower greatly the mortality and morbidity rates in any group. Let our efforts, then, be devoted to securing the benefits that may be had by such service rather than to acrimonious debates concerning odious comparisons. Let us avoid, furthermore, exaggeration of our difficulties for purposes of propaganda leading to unnecessary expenditures and appropriations.

1. Newsholme, Arthur: International Studies on the Relation Between the Private and Official Practice of Medicine with Special Reference to the Prevention of Disease, conducted for the Milbank Memorial Fund, London, George Allen and Unwin, Ltd., Baltimore, Williams & Wilkins Company 1:41, 1931.
2. Lowrie, R. J.: The Maternal Mortality Rate Computed and Standardized by a New Method, New York State J. Med., Oct. 1, 1931.

THE CREDIBILITY OF NARCOTIC ADDICTS

The issues in a case at law sometimes may turn on the ability of the judge and the jury to appraise correctly the weight to be given the testimony of a narcotic addict. Is every narcotic addict hopelessly given to fabricating fairy tales, a pathologic or inveterate liar who lies even when he has no personal end to gain by doing so? Do narcotic addicts habitually live in a world of fancy, so that no matter how much they may wish to do so they cannot observe accurately and report correctly what goes on about them? Persons to whom these problems are matters of concern, and particularly those engaged in the administration of justice, will find them lucidly, dispassionately and cogently discussed in an opinion filed by Judge Henry Clay McDowell, of the United States District Court for the Western District of Virginia, in *Kelly* v. *Maryland Casualty Company*,[1] and adopted by the United States Circuit Court of Appeals, Fourth Circuit.[2] An abstract appears in this issue of THE JOURNAL.[3]

Judge McDowell was confronted by a medical problem: Should he or should he not permit the introduction of evidence of the use of morphine by a witness in a case on trial, for the purpose of discrediting her tes-

1. 45 Fed. (2d) 782.
2. 45 Fed. (2d) 788.
3. Narcotic Addiction as Affecting Veracity, this issue, page 1917.

timony? He went boldly outside the sources of information to which judges ordinarily resort and personally consulted such medical books as were available. The value of his written opinion is enhanced by his citations to the medical books he consulted and by his quotations from them. To a lawyer it may seem dangerous for a judge to base a ruling on what he has read in medical books not admitted as evidence. The rules of evidence almost everywhere forbid the introduction of such books as proof of the facts and theories stated in them. An apparent exception to the general rule denying the admissibility in evidence of medical books is sometimes made where an expert witness testifies that he bases his opinion on the work of a particular author. In such a case, however, the particular work may be introduced in evidence solely for the purpose of contradicting and thereby discrediting the witness. In the present case, so far as the record shows, the books consulted were not offered in evidence by the parties to the cause and they had no opportunity of advising or objecting with respect to their use. Probably the greatest danger in the method adopted by Judge McDowell, however, lies in the paucity of medical books ordinarily available to a judge for consultation and in his limited ability to appraise unaided the weight of the statements of fact and of opinion in the books that he consults. It is one thing for a judge to consult a law book for guidance, and another and quite a different thing for him to consult a medical book. Any law book that is likely to be consulted is based on authority, and the sources of such authority are stated, so that the accuracy of the book can be determined by any competent lawyer. In medicine, however, there are no "authorities" comparable to the authorities in the legal world, and the value of a medical book depends on the knowledge, skill, experience and moral courage of the writer, with none of which the average judge is apt to be acquainted. From a legal point of view the very fact that the book of any given medical writer is consulted as a possible basis for a legal decision makes the author a witness—a secret witness unless the parties to the cause are fully advised concerning the matter—a witness not under oath and not subject to cross-examination, whose testimony is by those very circumstances inadmissible.

The course adopted by Judge McDowell, however, wisely pursued as he seems to have pursued it, is a course that should no doubt be encouraged. Probably the best plan for any judge to follow, if he desires to emulate Judge McDowell's example, would be to seek guidance through the nearest available organized medical library, or through the state or county medical association, or even through the American Medical Association. Possibly the day may come when judges will be provided with the aid of official medical advisers to help them over the difficulties that beset the nonmedical reader when he tries to find his way through the mazes of medical bibliography.

Current Comment

PREPARING A PEDIGREE

The importance of heredity in relation to disease is generally recognized. Unfortunately, however, few realize that the study of heredity is a scientific problem and that the language and technic of studies in heredity are specific to that science. A study of heredity charts in various periodicals will indicate to any observer the necessity for uniformity in the use of various symbols and the desirability of completeness. Since heredity charts are likely to be used fifty or a hundred years after they are first prepared as well as at the time of their first publication, and since they are likely to be studied by investigators in various parts of the world, the need for simplicity and accuracy becomes still more apparent. The Eugenics Society of Great Britain [1] has prepared for those especially interested a pamphlet entitled "How to Prepare a Family Pedigree" and a book of forms, charts and directions to be used by those who undertake such studies. The forms are concise; the directions take into account all the considerations that have been mentioned. The current tendency in medicine toward greater attention to problems of constitution and heredity indicates still further the desirability of this material.

SIR DAVID BRUCE

The cabled news of the daily press announced the death, November 27, of Major General Sir David Bruce in England at the age of 76 years. Sir Ronald Ross, himself one of the distinguished investigators of our day, is said to have described Bruce as one of the medical geniuses who served the British Empire. He will long be remembered for his contributions to our knowledge of trypanosomiasis, or African sleeping sickness. The malady has long been known; indeed, there are references more than two hundred years old mentioning a sleeping distemper among Negroes of the Guinea coast. Not until the present century was the etiology of this disease put on a sound basis. First, actively moving bodies were observed in the blood of patients. The motile agents were presently identified as trypanosomes. It was the merit of Bruce and his co-workers to have demonstrated that there are insect vectors for the causative micro-organisms, tsetse flies being the offenders. The so-called Gambian sleeping sickness is now widely distributed in the tropical zone of Africa. As first shown by Bruce, the Gambian parasite, Trypanosoma gambiense, is normally transmitted by the tsetse fly Glossina palpalis, and its distribution is now almost coincident with the range of this species. According to Hegner,[1] the indications at present are that Trypanosoma gambiense and Trypanosoma rhodesiense, the recognized organisms of African sleeping sickness, are usually transmitted by the tsetse flies belonging to the species Glossina palpalis and Glossina morsitans. Other species of the genus

1. How to Prepare a Family Pedigree, issued by the Eugenics Society, 20, Grosvenor Gardens, London, S. W. 1; price, sixpence.
1. Hegner, R. W.: The Transmission of Human Protozoa, Science 68:28 (July 9) 1926.

Glossina may perhaps serve as vectors under favorable circumstances. The etiologic factor of Malta fever was described by Bruce as Micrococcus melitensis in 1887. This, too, was an epoch-making discovery among what Garrison has termed "the chief glories of nineteenth century medicine." During the World War the studies of a British committee under Sir David Bruce working under field conditions in France contributed to the important demonstration that trench fever is a louse-borne disease.

Association News

MEDICAL BROADCAST FOR THE WEEK

American Medical Association Health Talks

The American Medical Association broadcasts from 2:25 p. m. to 2:30 p. m. on Monday, Wednesday and Friday over Station WBBM (770 kilocycles, or 389.4 meters), of the Columbia Broadcasting System.

The program for the week is as follows:

December 21. Infantile Paralysis.
December 23. Sleep and Growth.
December 25. No broadcast.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION, PUBLIC HEALTH, ETC.)

ARKANSAS

License Revoked.—The license to practice medicine of Dr. Thomas B. Sylar, Lepanto, was revoked by the State Medical Board of the Arkansas Medical Society at its regular meeting, November 10-11. Dr. Sylar was convicted and sent to the U. S. Penitentiary at Leavenworth, Kan., for violating the Harrison Narcotic Act.

Society News.—The Craighead-Poinsett County Medical Society entertained the First Councilor District and Northeast Arkansas Medical Society at Jonesboro, recently; the program included papers by Drs. Darmon A. Rhinehart, Little Rock, president, state medical society, on "Trends in Medicine"; Lee V. Parmley, "Medical Legislation," and Dr. Robert J. Haley, Jr., Paragould, "Early Diagnosis and Surgical Treatment of Perforated Gastric Ulcers."——Among others, Dr. Robert L. Sanders, Memphis, addressed the Second Councilor District Medical Society, Batesville, recently, on "Troublesome Cervix Uteri as Seen by the General Practitioner."

CALIFORNIA

Health at San Diego.—Telegraphic reports to the U. S. Department of Commerce from eighty-two cities with a total population of 36 million, for the week ended December 5, indicate that the highest mortality rate (19) appears for San Diego, and the rate for the group of cities, 10.8. The mortality rate for San Diego for the corresponding period last year was 16.7, and for the group of cities, 11.8. The annual rate for eighty-two cities for the forty-nine weeks of 1931 was 11.8, as against a rate of 11.9 for the corresponding weeks of 1930. Caution should be used in the interpretation of weekly figures, as they fluctuate widely. The fact that some cities are hospital centers for large areas outside the city limits, or that they have a large Negro population, may tend to increase the death rate.

Society News.—The San Francisco Heart Committee held its second annual graduate symposium on heart disease, November 19, sponsored by the San Francisco county medical and tuberculosis associations and the Health Council of the San Francisco Community Chest; a clinical pathologic conference also featured the meeting. Officers elected at this session include Drs. Arthur L. Bloomfield, chairman, and William C. Munly, secretary.——The Santa Barbara County Medical Society was addressed, October 12, by Drs. Ira B. Bartle, San Luis Obispo, on "Actinomycosis," and Henry J. Profant, Santa Barbara, on "Management of Mastoiditis and Petrositis."——A recent meeting of the Stanislaus County Medical Society, Modesto, was addressed by Dr. Joseph Catton, San Francisco, on "Medical Aspects of Recent Murder Cases."——The October meeting of the Monterey County Medical Society at Monterey was addressed by Dr. Edwin Schultz, Stanford University, on "Recent Advances in Poliomyelitis."——Dr. Carl R. Howson, Los Angeles, addressed the San Bernardino County Medical Society, San Bernardino, October 6, on "The Future of Medicine."——Dr. Dean Lewis, Baltimore, will address the Los Angeles Surgical Society, December 30, on "The History and Development of the Surgical Clinic."——Among others, Dr. Eldon W. Tice addressed the Los Angeles Obstetrical and Gynecological Society, December 8, on "Effect of Hot and Cold Packs on Blood Pressure in Abdominal Surgery," and Dr. Philip A. Reynolds, "Friedman Test for Diagnosis of Pregnancy."——Dr. Carl R. Howson, Los Angeles, was elected president of the Southern California Medical Association at its recent annual meeting; Drs. Harry E. Henderson, Santa Barbara, and Robert E. Ramsay, Pasadena, vice presidents, and Robert William Langley, Los Angeles, secretary. The next session will be held in Santa Barbara in April.——The San Francisco Pathological Society was addressed, December 7, by Drs. William H. Probert, Poughkeepsie, N. Y., and William T. Cummins on "Carcinoma of the Thyroid with Metastases"; P. Smith, "Retropleural Neurocytoma"; Dorothy A. Wood and Frederick L. Reichert, "Congenital Hemihypertrophy of the Leg with Neurofibromatosis"; Adelbert M. Moody, "Normoblasts in the Chorionic Villi in Early Pregnancy," and James F. Rinehart, "Studies on the Hemoglobin of Erythrocytes."

CONNECTICUT

Society News.—The Waterbury Medical Association was addressed, November 12, by Dr. James J. Hennessy, Waterbury, on "Treatment of Tuberculosis by Artificial Pneumothorax." Dr. John D. Booth, Danbury, gave a demonstration of the treatment.

Campaign to Prevent Colds.—With the cooperation of the student body and the faculty, the college board of health of Connecticut College, New London, has begun a campaign to prevent colds. Katharine Blunt, Ph.D., president of the college, is head of the board in conjunction with Dr. Mary K. Benedict, resident physician. It is proposed to build up resistance so that there may be as little susceptibility to colds as possible; to treat colds at the very start, thereby preventing their development, and to prevent those who do get colds from spreading them among the others. Instructions are placed in the dormitories and the students have been asked to go to the infirmary at the first suggestion of a cold so that treatment may be given before the cold develops. Students with colds will be kept in the dormitory until the danger of infecting others has been removed.

DISTRICT OF COLUMBIA

Personal.—Dr. Arthur C. Christie, president of the Medical Society of the District of Columbia, was elected president of the board of trustees of American University, Washington, November 2.——Dr. Radford Brown of Sloane Hospital for Women, connected with Columbia University, New York, has been appointed professor of obstetrics and gynecology and executive officer of the department in the George Washington University Medical School; he will assume his new duties, January 1.

New Building at George Washington University.—Construction will soon begin on a four-story addition to George Washington University Medical School, Washington. The building, which will cost about $75,000, will contain a central laboratory for the hospital, teaching laboratories for clinical microscopy, bacteriology and hygiene and preventive medicine, research laboratories for bacteriology, and animal quarters for experimental work for the entire school in addition to other research laboratories. This building will serve as temporary quarters until the medical school can move into a new plant, as a part of the proposed George Washington University Medical Center.

Medical Inspection of School Children.—According to the report made by a survey group of the public health committee of the Washington Board of Trade, medical inspection of schools in Washington is adequate so far as public service reasonably can be expected to extend. However, further medical and dental care of children provided by private means was recommended by a subcommittee. A survey of public bathing pools showed that all necessary steps for assuring sanitation

are being carried out. The results of a survey of ways and means of promoting greater safety for the public in the handling of motor traffic are to be announced later.

ILLINOIS

Personal.—With the creation of a new health office, that of county epidemiologist, the position of health officer of DuPage County has been discontinued. William V. Hopf, D.D.S., Lombard, who was the health officer, will assume the duties of the new office.

Society News.—The Fulton County Medical Society was addressed, December 1, in Canton, by Dr. Frank E. Simpson, Chicago, on the use of radium in malignant tumors, and Dr. Paul G. Dick, Chicago, treatment of malignant conditions with X-rays; Dr. Josiah J. Moore, also of Chicago, gave a demonstration of the Canti cancer film. —— Drs. Bransford Lewis and Alphonse McMahon, both of St. Louis, addressed the Sangamon County Medical Society, Springfield, December 3, on "A Survey of Urology for the General Practitioner" and "Differential Diagnosis Between Early Tuberculosis and Hyperthyroidism," respectively.——Dr. Samuel M. Feinberg, Chicago, addressed the Rock Island County Medical Society, December 8, on "Allergy in General Practice." —— Dr. Frederick A. Baumgart was elected president of the newly created Danville Medical Society, and Dr. George T. Cass, secretary.——The Jo Daviess County Medical Society was addressed at Warren recently, among others, by Dr. Karl B. Rieger, Freeport, on "Thrombo-Angiitis Obliterans."——The Clinton County Medical Society was addressed at Carlyle, November 17, by Drs. William S. Carter, Trenton, and J. P. Murphy on "Otitis Media, Middle Ear Infection" and "Relation of Eyestrain and Headaches," respectively.——At the meeting of the Perry County Medical Society, December 3, Dr. Frank F. Maple, Chicago, spoke on "Abortion and Its Treatment," and Dr. James H. Hutton, Chicago, "Recent Advances in Endocrinology."

Chicago

Society News.—Edwin O. Jordan, Ph.D., was elected president of the Institute of Medicine of Chicago at its annual meeting, December 1; Dr. Arthur R. Elliott, vice president; Dr. George H. Coleman, secretary, reelected; Dr. John Favill, treasurer, and Dr. Ludvig Hektoen, chairman of the board of governors. Dr. Otto L. Schmidt gave the presidential address on "The Rôle of Medical and Hygienic Museums in Education."——Dr. Morris Fishbein addressed the Historical Club of the University of Illinois College of Medicine, December 2, on "The Future of Medicine." —— The Chicago Gynecological Society was addressed, December 18, by Drs. Milton J. Summerville and Frederick H. Falls on "A Critical Study of the Technic and Clinical Value of the Sedimentation Rate in Gynecology"; Jacob P. Greenhill, "Thymophysin and Weak Pituitary: Comparison in 40 Cases," and Richard A. Lifvendahl, "A Sign for the Detection of Small Amounts of Free Blood in the Abdomen."——The Chicago Pediatric Society was addressed, December 15, among others, by Dr. Henry E. Irish on "Effect of Cod Liver Oil-Skimmed Milk Feeding on Bones After One Year."——The Chicago Neurological Society was addressed, December 17, among others, by Dr. Isadore Pilot on "Putrid Brain Abscess—Its Pathogenesis."——At the meeting of the Chicago Society of Allergy, December 21, Dr. Harry L. Huber, among others, will speak on "Dermatitis Due to Burweed Marsh Elder."——Drs. Thomas D. Allen and Ramon Castroviejo will address the Chicago Ophthalmological Society, December 21, on "The Autonomic Nervous System and the Eye" and "A New Knife for Ophthalmic Surgery," respectively.

KANSAS

Photographic Service.—The photographic department of St. Francis Hospital, Wichita, recently announced that its service is available to all physicians who desire it. The work will be done on a cost basis, a charge of $1 having been decided on for one photograph. The service comprises the production of clinical photographs of patients and gross specimens, photomicrographs, the copying of charts, drawings and printed or typewritten data, and the making of lantern slides. The photographic department is supervised by the pathologist of the hospital, although it is operated as an independent unit.

Society News.—The Labette County Medical Society was addressed, November 18, by Drs. Earle G. Brown and William C. Menninger, Topeka, on infantile paralysis.——The Franklin County Medical Society was addressed, November 21, by Drs. Sherwin E. Mella and Robert Lee Hoffmann, both of Kansas City, on "Diagnosis and Treatment of Common Skin Diseases" and "Urology," respectively.——The Wyandotte County Medical Society was addressed, November 14, by Drs. Elam A. Reeves, Kansas City, on "Placenta Praevia"; Earle G. Brown, Topeka, "Epidemiology of Infantile Paralysis," and James R. Elliott, Kansas City, Mo., "Management of Poliomyelitis During the Stage of Recovery."——The Harvey and Sedgwick county medical societies, in joint session at Newton, were addressed, November 3, by Drs. Arthur Steindler, Iowa City, on hip and back sprains and their connection with compensation cases, and James A. Wheeler, Newton, vitamins. Dr. Henry N. Tiben, Wichita, addressed the Sedgwick County Medical Society, November 20, on "Medical Organization."

MICHIGAN

Personal.—Dr. Alden G. Sheets has been appointed health officer of Eaton Rapids.——Dr. Lloyd S. Dunkin has been appointed health officer of Greenville to succeed the late Dr. Will H. Lester.

Dr. Moll Honored.—The Genesee County Medical Society tendered a testimonial dinner, October 28, to Dr. Carl F. Moll, Flint, president of the Michigan State Medical Society. The toastmaster was Dr. Frank E. Reeder. The program included talks by Dr. Moll; Dr. Frederick C. Warnshuis, Grand Rapids, on the state medical society; Judge V. W. Dodge, the physician and the probate court; Dr. Clyde C. Slemons, Grand Rapids, the physician and the state board of health, and Dr. Leslie L. Willoughby, the Genesee medical society.

Society News.—Dr. James D. Bruce, Ann Arbor, addressed a joint meeting of the Berrien County Medical Society and the dentists of the county, November 23, on "Focal Infections and Their Relations to Systemic Disease."——A symposium on infantile paralysis featured the meeting of the University of Michigan Pediatric and Infectious Disease Society, Ann Arbor, November 19-20. —— Dr. Ralph Pemberton, Philadelphia, addressed the medical section of the Wayne County Medical Society, December 8, on "The Newer Outlook on Chronic Arthritis."——Dr. Harry W. Plaggemeyer, Detroit, addressed the Hamtramck Medical Society, November 20, on the activities of the Wayne County Medical Society.——Judge Charles B. Collingwood, Lansing, addressed the Calhoun County Medical Society, December 1, on "The Doctor in Court."——The Washtenaw County Medical Society, Ypsilanti, conducted a symposium on cancer at its meeting, November 24; the speakers included Drs. Frank L. Rector, Evanston, Ill., Max Ballin, Detroit, and Conrad Georg, Sr., Eugene B. Potter and Mark Marshall, all of Ann Arbor; Dr. George F. Inch addressed the society, among others, December 11, on "Importance and Necessity for Early Diagnosis and Treatment of Mental Cases."—— Dr. William H. Alexander, Iron Mountain, addressed the Dickinson-Iron County Medical Society, December 3, on "Some Surgical Problems in Pulmonary Tuberculosis."——Dr. Karl A. Menninger, Topeka, Kan., addressed a joint meeting of the Wayne County Medical Society and the Detroit Society of Neurology and Psychiatry, December 15, on "Focal Suicide: Psychogenic Aspects of Physical Disease."

MINNESOTA

Personal.—Dr. Jay Arthur Myers has recently been promoted from associate professor to professor of preventive medicine at the University of Minnesota School of Medicine, Minneapolis.——Dr. Lincoln A. Sukeforth, public health director of Duluth, has retired after eight years' service.—— Dr. Joseph A. Roy, Red Lake Falls, was elected mayor of that city in November.

Licenses Revoked.—At a meeting of the Minnesota State Board of Medical Examiners in St. Paul, November 10, the license of Dr. John Gerardi Halland, Motley, was revoked because of his habitual indulgence in the use of drugs. The license of Dr. David Gordon, Minneapolis, was also revoked at this meeting as the result of his conviction on nine counts of violating the Harrison Narcotic Act. Dr. Gordon was sentenced to eighteen years' imprisonment at Leavenworth. This was his second offense.

Society News.—Dr. Emil S. Geist, Minneapolis, addressed a joint meeting of the West Central and Kandiyohi-Swift county medical societies recently on "Treatment of Fractures." —— The Washington County Medical Society was recently addressed by Drs. John C. McKinley, Minneapolis, and Wallace H. Cole, St. Paul, on infantile paralysis.——Dr. Frederic E. B. Foley, St. Paul, addressed the Minnesota Academy of Medicine, December 9, on "Embryology and Surgical Correction of Certain Renal Malformations." Dr. Irvine McQuarrie, Minneapolis, gave a thesis on "Some Recent Observations Regarding the Nature and Treatment of Epilepsy in Children."

V 19

MISSOURI

Personal.—The Missouri Commission for the Blind recently announced that Dr. Meyer Wiener had resigned as director of the department for the prevention of blindness, which he established in 1929. Dr. Wiener is associate professor of clinical ophthalmology in Washington University School of Medicine, St. Louis.——The library of Dr. Thomas J. Downing, New London, has been given to the St. Louis Medical Society by Mrs. Downing in compliance with a request of the physician before his death, Dec. 7, 1930. The collection consists of 743 volumes.

Society News.—Dr. Horace W. Soper, St. Louis, entertained four of his classmates in Washington University School of Medicine at a dinner, November 17, given in honor of Dr. George B. Tuttle, Kalaupapa, Hawaii. The physicians were Drs. Tuttle, Albert E. Taussig, Adolph G. Schlosstein and Edward J. Goodwin, St. Louis. Dr. Tuttle addressed the St. Louis Medical Society, among others, November 10, on "Leprosy in Hawaii."——At the December 8 meeting of the St. Louis Medical Society, Dr. Russell A. Hennessey, Memphis, Tenn., spoke on "Traumatic Lesions of the Urinary Organs," and Drs. Howard L. Stitt and Charles E. Wooding, Cincinnati, discussed "Bronchial Lavage and Its Medical Aspects." —— The Kansas City Southwest Clinical Society held its monthly clinic at the Kansas General Hospital, December 8, when Dr. Morris Fishbein, Chicago, spoke on "The Trend in Medical Practice." The evening session in conjunction with the Jackson County Medical Society was addressed by Dr. Quitman U. Newell, St. Louis, on "Five-Year End-Results in the Treatment of Carcinoma of the Uterine Cervix." —— The Twenty-Sixth District Medical Society was addressed, November 17, among others, by Bruce E. Ratcliff, D.D.S., Springfield, on "Teeth as Foci of Infection—Diagnosis and Treatment," and Dr. Duff S. Allen, St. Louis, "Thyroid Toxicosis."

NEW JERSEY

Dr. Theobald Smith Honored.—The Rockefeller Institute for Medical Research gave a dinner, November 20, at the department of plant and animal pathology near Princeton in honor of Dr. Theobald Smith, for many years director of the department. The occasion marked the opening of the Theobald Smith House, which was for many years the residence of Dr. and Mrs. Smith and has now been remodeled as a staff house for scientific workers. Dr. Simon Flexner, New York, director of the institute, presided at the dinner and addresses were made by Dr. William H. Welch, Baltimore, John D. Rockefeller, Jr., and Dr. Smith. Ground has recently been broken for the erection of new buildings for the division of plant pathology (THE JOURNAL, June 20, p. 2131). There will be a laboratory building two and a half stories high, eight greenhouse units and potting sheds. The name of the Princeton branch has been changed to the Department of Plant and Animal Pathology of the Rockefeller Institute for Medical Research.

NEW YORK

New State Hospital.—Dr. William J. Tiffany, superintendent of Kings Park State Hospital since 1928, has been appointed superintendent of the new Pilgrim State Hospital, Brentwood, the first units of which have recently been opened for the reception of patients. Accommodations for 1,000 patients are now ready and 480 have already been received. It is expected that the project will be completed in the summer of 1932. There will then be eighteen buildings, erected at a cost of about $20,000,000, with a capacity for 6,600 patients. The hospital is named for Dr. Charles W. Pilgrim, Central Valley, for many years superintendent of the Hudson River State Hospital, Poughkeepsie, and at one time chairman of the former state hospital commission. Dr. Tiffany has been in the state hospital service since 1904, except for a short period at St. Joseph's Hospital, Paterson, N. J.

Clinics on Cancer.—The tumor clinic of the Memorial Hospital, Albany, is conducting a series of monthly clinical meetings on cancer for all physicians interested. Each meeting begins with a clinicopathologic conference, followed by discussion of the incidence, history and classification of cancers of the region under study for the day and later by a tumor clinic and round table discussion of cases. For evening sessions, addresses by visiting physicians have been arranged. The first two were given by Drs. Ernest M. Daland, Boston, November 4, on "Importance of the Tumor Clinic in the Cancer Problem," and Burton J. Lee, New York, December 2, "Early Diagnosis and Treatment of Cancer of the Breast." Future lectures will be by Drs. George M. MacKee, New York, Jan. 6, 1932, on cancer of the skin; William P. Healy, New York, February 3, cancer of the female generative organs; Benjamin S. Barringer, New York, March 2, cancer of the urinary tract; Louis C. Kress, Buffalo, April 6, bone tumors, and Lloyd F. Craver, New York, May 4, medical treatment of the cancer patient. Dr. Brayton E. Kinne, Albany, is executive director of the tumor clinic.

New York City

New Red Cross Building.—The New York Chapter of the American Red Cross celebrated the twenty-fifth anniversary of its founding, November 5, with the dedication of a new twelve-story chapter house at Lexington Avenue and Thirty-Eighth Street. The house was built with funds from the Conrad Hubert Fund, administered by former Gov. Alfred E. Smith, former President Calvin Coolidge and Julius Rosenwald, Chicago philanthropist. Among speakers at the ceremony were John Barton Payne, chairman of the central committee of the Red Cross, Washington, D. C.; Dr. Livingston Farrand, president of Cornell University; John H. Finley, associate editor of the New York *Times*, and former Governor Smith.

Society News.—Members of the laboratory staffs of the hospitals in the Bronx and representatives of the medical examiner's office recently organized the Bronx Pathological Society, with Drs. Joseph Felsen as president; Charles H. Hochman, vice president, and William Aronson, secretary. Dr. James Ewing addressed the first meeting, December 15, on "The Place of Pathological Anatomy in Modern Medicine," and Dr. Felsen, "Tumors of the Colon and Rectum." —— Dr. Theodore H. Weisenburg, Philadelphia, addressed the New York Physical Therapy Society, December 9, on "Physical Therapy in Diseases of the Nervous System."——Dr. Walter B. Cannon, Boston, addressed the section on neurology and psychiatry of the New York Academy of Medicine, December 8, on "The Autonomic Nervous System and Its Chemical Mediators."——A meeting of the New York Electrical Society, December 16, was devoted to discussions of the uses of electricity in medicine. Dr. Howard A. Kelly, Baltimore, presided and the following speakers gave addresses: Gioacchino Failla, Sc.D., Memorial Hospital, on the use of high voltage roentgen rays in the treatment of cancer; Drs. Charles F. Tenney, Jr., Fifth Avenue Hospital, on the fever-producing machine; Grant E. Ward, Johns Hopkins University Medical School, Baltimore, the so-called radio knife, and Horatio B. Williams, professor of physiology, Columbia University College of Physicians and Surgeons, the electrocardiograph.

NORTH DAKOTA

Unlicensed Practitioner Sentenced.—Robert G. Errington, who has operated in Fargo as a naturopath and "cancer specialist," advertising his offices as a "nature clinic," was sentenced, October 30, to spend thirty days in jail and to pay a fine of $300. He was committed to the Cass county jail pending the filing of an appeal bond, which was set at $1,000. In passing sentence, Judge P. M. Paulsen is reported to have said that Errington had openly defied the law not only in North Dakota but in other states. THE JOURNAL in 1928 reported that Errington had been found guilty of violating the basic science law of Minnesota and was fined $500 and costs. He had previously been sentenced in the same state to five months in jail for violating the medical practice act. According to the secretary of the state medical association, several persons have recently complained that Errington not only guaranteed cures, for which large sums of money were paid in advance, but had sued them on notes given by them in addition to the cash advances.

OREGON

Personal.—Dr. Henry H. Dixon, formerly of Denver, has joined the faculty of the University of Oregon Medical School as professor of neuropsychiatry.——Dr. Edward A. Weir has been appointed supervisor of public health activities for the U. S. Public Health Service in the district of Portland to succeed Dr. Frank S. Fellows, who was recently appointed district medical director of Alaska.——Dr. Josiah Morris Slemons, Los Angeles, addressed the Polk-Yamhill-Marion Counties Medical Society, Salem, November 10, on "Induction of Labor at Term."

PENNSYLVANIA

Society News.—At the meeting of the Delaware County Medical Society, December 10, Drs. Owen J. Toland, Philadelphia, and Aaron Lovett Dewees, Ardmore, spoke on "Prophylactic Obstetrics" and "Technic of Contraception," respectively. ——Dr. Arthur F. Coca, New York, lectured in Pittsburgh on "Classification of Allergic Diseases with Reference to Diagnosis and Treatment," November 24, under the auspices of Monte-

fiore Hospital.——Drs. James K. Everhart and Henry T. Price, among others, addressed the Pittsburgh Academy of Medicine, December 8, on "Transfusion in Infancy," and "Leukemia in Children," respectively.——Dr. Jesse O. Arnold, Philadelphia, addressed the Lycoming County Medical Society, Williamsport, December 11, on "Cause and Control of Eclampsia."

Philadelphia

Changes at Temple University.—Dr. Hugo Roesler, formerly of the University of Vienna, Austria, was recently appointed assistant professor of radiology at Temple University School of Medicine. Recent promotions include those of Drs. George W. Deitz, to associate professor of cardiovascular diseases of children; Edward C. Davis, to assistant professor in proctology; Thomas Carroll Davis, to assistant professor in rhinolaryngology and Samuel Goldberg, to clinical professor of pediatrics.

Society News.—The Philadelphia Association of Retail Druggists entertained Philadelphia physicians at a smoker, December 4. Addresses on the cooperation of the two professions were delivered by Drs. George C. Yeager, W. Burrill Odenatt and John O. Bower, and Prof. Ernest Fullerton Cook, Pharm.M., among others.——A symposium on juvenile delinquency was conducted at the meeting of the Philadelphia Psychiatric Society, December 11. Speakers were Drs. Frederick H. Allen, Samuel Leopold and James S. Plant, Newark, N. J., and Judge Paul N. Schaeffer, Reading.——Dr. Abraham Flexner, New York, addressed the College of Physicians of Philadelphia, December 14, on "The Graduate School and Full Time Teaching."——Dr. Charles E. G. Shannon delivered the postgraduate seminar of the Philadelphia County Medical Society, December 11, on squint as encountered by the general practitioner.—— Dr. Hubley R. Owen addressed the Philadelphia Academy of Surgery, December 7, on "The Problem of Delayed Union and Ununited Fractures."——Drs. Hugh W. Josephs, Baltimore, and David L. Drabkin addressed the Philadelphia Pediatric Society, December 8, on "Nutritional Anemia: Its Prevention and Treatment" and "Recent Progress in Experimental Anemia," respectively.——The annual banquet of the Medical Alumni Association of the Medico-Chirurgical Society of Philadelphia was held, November 19. Dr. John J. Dailey, McAdoo, was elected president.—— Dr. John A. McGlinn, among others, addressed the Obstetrical Society of Philadelphia, December 3, on "Reconstruction of the Urethra."—— Dr. Louis Edeiken, among others, addressed the Philadelphia Roentgen Ray Society, December 3, on "Stimulating Doses of X-Rays for Amenorrhea and Sterility."——Dr. George E. de Schweinitz addressed the American Philosophical Society, December 4, on "Toxic Amblyopias with Especial Reference to Methyl Alcohol."

SOUTH CAROLINA

Society News.—Among speakers before the Fifth District Medical Society, Chester, November 1, were Drs. Robert W. McKay, Charlotte, N. C., on "Urological Problems of the General Practitioner"; William J. Henry, Chester, "Glandular Fever," and Hugh P. Smith, Greenville, "Primary Hypochronic Anemia."

Grant for Research on Goiter.—Bernard M. Baruch, New York, has recently given $13,000 to the South Carolina Food Research Laboratory at the Medical College of the State of South Carolina, Charleston, for investigations into the relation of diet to simple goiter. Seasonal and other variations in the amount of iodine available normally in the environment of persons in goitrous and nongoitrous regions will be studied. Goiter is not endemic in South Carolina.

TENNESSEE

Society News.—Dr. George I. Baker addressed the Knox County Medical Society, Knoxville, November 17, on "Management of Diabetes in Children." Dr. Harvey J. Howard, St. Louis, addressed the society, November 23, on "Mechanism of Defense of the Mucous Membrane."——Dr. Richard A. Barr addressed the Nashville Academy of Medicine, November 17, on appendicitis, with a review of 500 cases subject to operation. Other recent speakers have been Drs. John S. Cayce, November 3, on "Treatment of Hyperemesis Gravidarum," and William R. Cate, November 10, "Relationship of Hypertension and Nephritis."—— Dr. John E. Frazier, Newbern, was elected president of the Walnut Log Medical Society, comprised of physicians of western Kentucky and Tennessee, at its meeting, November 13-14, at Walnut Log, on Reelfoot Lake. Among speakers at the meeting were Drs. Willard Bartlett, St. Louis, on "Results of Experience with Barbituric Acid Compounds for Surgical Anesthesia"; Peter Whitman Rowland, Jr., Memphis, "Immediate and Ultimate Prognosis of Certain Types of Cardiovascular Disease"; William T. Black, Memphis, "Differential Points in Diagnosis of Pelvic Masses," and Ernest H. Baird, Dyersburg, "Diseases of the Gallbladder."——The Tennessee Hospital Association will hold its annual meeting jointly with the Kentucky Hospital Association at Memphis in April, 1932, it has been announced.——Drs. Perry Bromberg and Samuel S. Riven, Nashville, addressed the Blount County Medical Society, Maryville, November 14, on "Renal Calculi" and "Thyroid Heart," respectively. The Knox and Monroe county medical societies were guests at the meeting.—— Dr. John S. Freeman, Springfield, was elected president of the Middle Tennessee Medical Society, at its seventy-fourth semiannual meeting, November 6, at Fayetteville. The next meeting will be held in Sparta in May, 1932.——Dr. Edward C. Mitchell, Memphis, among others, addressed the medical society of Hardin, Lawrence, Lewis, Perry and Wayne counties, Savannah, October 22, on pyelitis and other diseases of the kidney.——Dr. Howard P. Hewitt addressed the Chattanooga and Hamilton County Medical Society, November 12, on "Prenatal Care and Management During Labor and Puerperium."——Dr. James L. Morton, Shelbyville, addressed the Bedford County Medical Society, November 19, on apoplexy.

TEXAS

License Revoked.—The license of Dr. Pedro M. Hernandez, Corpus Christi, was revoked, November 20, by the judge of the one hundred and seventeenth district court of Nueces County in a suit brought by the state board of medical examiners. The suit was based on the allegation that the license was obtained by fraud in that Hernandez had represented himself as a graduate of the National University School of Medicine of Mexico, whereas he had not attended or graduated from that school.

WEST VIRGINIA

Personal.—Dr. Vinton A. Selby, Clarksburg, resigned, November 1, as health officer of Harrison County and was succeeded by Dr. Americus J. Kemper, Lost Creek.

Society News.—Dr. Haven Emerson, New York, conducted a two-day institute for health workers during the meeting of the West Virginia Public Health Association, held at Morgantown, November 19-21. His subjects were "Preventable Disease from the Standpoint of the Public Health Official and the Medical Profession" and "Public Health Practices and Standards." Other speakers were Drs. John L. Lavan, Toledo, Ohio, on immunology, and Estella Ford Warner of the U. S. Public Health Service on the status of West Virginia's health program. Dr. William J. MacDonald, Wellsburg, was elected president and Dr. David Littlejohn, Charleston, secretary.—— Dr. John R. Caulk, St. Louis, addressed the Ohio County Medical Society, Wheeling, December 11, on "The Cautery-Punch Operation." Dr. David Silver, Pittsburgh, addressed the society, December 4, on "Future Progress in the Care of the Cripple."

GENERAL

Radiological Society Awards Medals.—Two gold medals for distinguished service in the field of radiology were awarded to physicians at the recent meeting of the Radiological Society of North America in St. Louis. Dr. Carlos Heuser, Buenos Aires, Argentina, who was the guest of the society for the meeting, received a medal in recognition of work in methods of making roentgenograms for the study of pregnancy. Dr. Maximilian J. Hubeny, Chicago, was awarded a medal in honor of his research on the determination of dental focal infection, the injection of the sphenoid sinuses with a suspension of barium sulphate and oblique projection in the examination of the lumbar spine. Dr. Francis Carter Wood, New York, was elected president and Dr. Byron H. Jackson, Scranton, Pa., was made president-elect of the society; Dr. Donald S. Childs, Syracuse, N. Y., was elected secretary. The officers will assume their stations January 1.

Operations for Removal of Cataracts in India.—A group of American surgeons plan to perform about 100 operations for the removal of cataracts each day in India during the winter months, according to a recent report. The work is under the direction of Dr. Henry T. Holland, Shikarpur, who holds an annual eye clinic at the Seth Heranand Charitable Eye Hospital. The American physicians include, it is reported, Drs. Walter I. Lillie, Rochester, Minn.; Oscar B. Nugent, Agnes Beulah Cushman and Louis Bothman, Chicago; Watson W. Gailey, Jr., Bloomington, Ill., and Joseph J. Hompes, Lincoln, Neb. Certain sections of northern India are said to be characterized by a greater prevalence of cataracts than any other section of the world; some of the causes for this condi-

tion are intense sunlight and lack of proper nourishment which creates premature senility. The British government pays the surgeons, and the operations cost the patient nothing. A group of specialists performs the operations; a second group fits the patients with glasses after the operations have been performed. It is planned to treat more than 5,000 natives, the report stated.

Society News.—The American Urological Association will hold its next annual meeting in Toronto, Canada, May 30-June 2.——At the annual meeting of the Association of American Medical Colleges in New Orleans, November 30-December 2, Dr. Louis B. Wilson, director of the Mayo Foundation of the Graduate School of the University of Minnesota, was elected president; Dr. Herman G. Weiskotten, dean, Syracuse University School of Medicine, vice president, and Dr. Fred C. Zapffe, Chicago, secretary, reelected. The next annual meeting will be held in Philadelphia.——The twelfth annual meeting of the American Student Health Association will be held in New York, December 29-30. Among speakers listed on the program are Drs. Shailer U. Lawton, New York, on "Infectious Conditions in Relation to Physical Activity"; Thomas K. Richards, Boston, "Prevention and Treatment of Knee and Ankle Injuries"; Jay Arthur Myers, Minneapolis, "Eleven Years' Observation on Tuberculosis among University Students," and Miliord E. Barnes, Iowa City, Iowa, "Health Examination of Food Handlers by University and College Health Services." Dr. Warren E. Forsythe, University of Michigan, Ann Arbor, is president of the association. ——At the recent annual meeting of the Central Neuropsychiatric Association, Dr. Karl A. Menninger, Topeka, Kan., was elected president; Dr. Hans H. F. Reese, Madison, Wis., vice president, and Dr. Henry W. F. Woltman, Rochester, Minn., secretary. The next meeting will be held in September, the location to be decided later.

Follow-Up Committee of White House Conference.—Two conferences of the Follow-Up Committee of Section I of the White House Conference on Child Health have already been held to consider the scope of its work and methods of carrying it out. The objects of the White House Conference were (1) to study the present status of the health and well being of the children of the United States; (2) to report what is being done for child health and protection, and (3) to recommend what ought to be done and how to do it. It was to carry out this third objective that the organization of the Follow-Up Committee was authorized at the last session of the White House Conference (THE JOURNAL, June 6, p. 1962). The survey made by Section I revealed that the gaps in child health service were of two kinds: failure to apply much that is known, and the necessity for further investigation in the clinic and laboratory that the needs in the promotion of child health may be more adequately met. The committee's first function is to try to stimulate a more adequate application of the known by advising constructively on and initiating principles of health betterment in the working programs of existing organizations active in the promotion of child health. The committee's purpose will be to invite the formulation and acceptance by all the agencies involved in promotion and protection of the health of the child of a central program embodying the basic principles on which are founded the physical and mental stamina of the people. It is hoped to continue this committee for ten years, which would bring it up to the probable next national child health conference. Members of the committee include Dr. Ray Lyman Wilbur, Washington, D. C., honorary chairman; Dr. Samuel McC. Hamill, Philadelphia, chairman; Dr. Fred L. Adair, Chicago; Dr. Kenneth D. Blackfan, Boston; Ida M. Cannon, R.N., Boston; Dr. Anton J. Carlson, Chicago; Dr. Samuel J. Crumbine, New York; Dr. Clifford G. Grulee, Chicago; Dr. Henry F. Helmholz, Rochester, Minn.; F. J. Kelly, Ph.D., Chicago; Guy S. Millberry, D.D.S., San Francisco; Dr. Fred Moore, Des Moines, Iowa; Sophie C. Nelson, R.N., Boston; Dr. Everett D. Plass, Iowa City; Richard E. Scammon, Ph.D., Rochester, Minn.; Dr. Wingate Todd, Cleveland; Dr. Philip Van Ingen, New York; Henry F. Vaughan, Dr.P.H., Detroit, and Dr. Borden S. Veeder, St. Louis.

LATIN AMERICA

Research on Leprosy.—An international center for research on leprosy is to be established in Rio de Janeiro by the Brazilian government in cooperation with the Council of the League of Nations, according to plans made at the session of the council in Geneva, September 1. The object is to undertake work that may contribute, by means of epidemiologic, clinical and biologic research, toward prevention and treatment. A specialized course of instruction open to scientists, members of the medical profession and hygienists of all countries is planned. The cost of the installation and upkeep of the institution is to be met by the Brazilian government, but gifts, legacies and grants will be welcomed. The plans are for five years, at the end of which time an extension may be proposed. The governing body for the center as contemplated will consist of the members of the health committee of the League of Nations with one representative of the donating government.

FOREIGN

New Journal of Diseases of Digestive System.—A bimonthly journal, *Archivio Italiano delle Malattie dell'Apparato Digerente*, appeared for the first time in October, in Bologna, Italy. The first issue contains ninety-six pages of original articles on topics related to conditions or diseases of the digestive system. Dr. C. Frugoni, Padua, is the editor and Drs. G. M. Fasiani, Padua, and A. Busi, Rome, associate editors.

Hughlings Jackson Fund.—In answer to an appeal from admirers of the late Hughlings Jackson, a fund of £1,110 has been subscribed to endow the triennial lecture of the neurological section of the Royal Society of Medicine. A die is now being executed by James Metcalfe for the medal, which will bear on the obverse side a portrait of Jackson. The first medal will be presented to this year's lecturer, Sir Charles Sherrington.

Bubonic Plague in China.—An unusually extensive spread of bubonic and pneumonic plague is being reported in the north China provinces of Shansi and Shensi. The first report of Dr. Percy T. Watson, director of the hospital at Fenchow, Shansi, showed that 100 villages were infected. Late in October Dr. Watson with fifteen members of his staff left for the plague-infected area, the nearest point of which is four days' journey west of Fenchow. It was stated that every year at this time bubonic plague breaks out in this region. The plague recedes in December, as cold weather diminishes rat-flea population. The mortality from bubonic plague in northern China is about 95 per cent. The Chinese government gives attention to plague prevention throughout the entire year. The Fenchow staff takes on the work at the request not only of the Shansi provincial legislature and governor but also of the Chinese national health administration; both these organizations provide funds for expenses. The Chinese national quarantine service sent three physicians in addition to the head of the department, Dr. Wu Lien Teh.

Government Services

Dr. Stiles Retires from Public Health Service

Dr. Charles Wardell Stiles, zoologist of the U. S. Public Health Service since 1902, retired from active duty, October 1. Dr. Stiles, a native of New York, received his early education at Connecticut Wesleyan University and studied later at various foreign universities, taking the degree of doctor of philosophy at Leipzig in 1890, and doctor of medicine from the University of Paris Faculty of Medicine in 1896. Many honorary degrees have since been conferred on him. Dr. Stiles began his service with the government in 1902 as consulting zoologist to the bureau of animal industry of the department of agriculture, and professor of zoology in the public health service. He has held teaching positions in medical zoology at Georgetown University, the Army Medical School, the Naval Medical School and Johns Hopkins University. From 1909 to 1914, he was scientific secretary of the Rockefeller commission for the eradication of hookworm. He is the author of many books relating to his specialty and recently finished a key catalogue of the parasites of men and animals, indexed in all the most important languages (THE JOURNAL, September 19, p. 860). Representatives of the public health service, the bureau of animal industry, the bureau of plant industry, the bureau of biological survey, U. S. National Museum, medical departments of the army and navy, Johns Hopkins University and other groups gave a dinner in honor of Dr. Stiles, October 7, at the Cosmos Club, Washington. Among the speakers were Drs. William H. Welch, Baltimore; William Sydney Thayer, Baltimore, and Arthur M. Stimson.

Appointments in Drug Control Unit

Drs. Northen O. Tribble, Atlanta, Ga., and Virgil S. McDaniel were recently appointed to fill vacancies in the drug control unit of the food and drug administration, U. S. Department of Agriculture. These vacancies were caused by the resignation of Dr. James J. Durrett, chief of drug control, and Dr. George E. Clarke, medical officer in drug control unit. Dr. Frederick J. Cullen was advanced to succeed Dr. Durrett. Dr. McDaniel was transferred from the U. S. Public Health Service.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 21, 1931.

Research on the Cause of Cancer

It may be remembered that in 1925 Dr. W. E. Gye, with the help of the microscopist Mr. J. E. Barnard, F.R.S., brought forward the theory that cancer is due to the cooperation of a virus (consisting of minute spheroids rendered visible by dark-ground illumination and photographed by ultraviolet rays) and a "specific factor." His researches attracted world-wide attention, but his theory was not considered established. Dr. Gye, however, was so convinced of its truth that he retired to the laboratories of the National Institute for Medical Research and now, after six years' patient work, has produced, in conjunction with Dr. W. S. Purdy, a book on the cause of cancer which embodies his later researches. The authors are satisfied, contrary to the prevalent view, that cancer is a parasitic disease. They attribute the difficulty of accepting their view to the complexity of the mechanism involved: two components of a widely different nature, neither of which can act alone. Dr. Gye has shown that malignant tumors can be produced in chickens by injecting extracts of tumors rendered free from cancer cells. He did this with the Rous sarcoma, verifying the results obtained by Rous. It has been argued, however, that Rous sarcoma is not a true cancer and that therefore the results are not applicable to the latter disease. Dr. Gye is now able to report that he has been able to extract from cancer a "something" which, when added to an extract of the Rous sarcoma treated in such a way as to destroy all virus or living organism, caused a growth when injected into a chicken. The deduction seems to be that the cancer also contains the living organism. This is the crucial experiment of the series, but it cannot yet be repeated with reasonable regularity. Hence it is concluded that "the question of the direct demonstration of viruses in new growths of mammals remains in a disappointingly inconclusive state. The subject has more than theoretical importance. There is an immediate practical aspect. If methods of handling mammalian viruses and of classifying them by immunity experiments could be discovered, then, since we have shown that large animals produce antiviral antibodies readily, the way to prophylactic immunization of man against cancer would be available." This is the immediate and urgent problem of cancer research. So far, the opinions of experts is guarded. Dr. J. A. Murray, director of the Imperial Cancer Research Fund Laboratory, says that Dr. Gye evidently recognizes the difficulties of the investigation and the extent to which the demonstration is not conclusive. Without a more careful consideration of Dr. Gye's new presentation of his views, Dr. Murray would not commit himself to any fuller statement. Professor McIntosh, director of the Cancer Research Laboratories, Middlesex Hospital, says: "The book is an important contribution to our knowledge of cancer."

Fewer Fatal Accidents

The continued attempts to reduce the fatal accidents from automobile traffic are at last bearing fruit. In the first nine months of this year there was a reduction of 10 per cent in accidents resulting in death, but a small increase was shown in other accidents. Last year an average of twenty persons a day were killed in the streets. In each of the last ten years the number has exceeded that of the previous year, but this year there were 293 fewer deaths than in the corresponding period of 1930. There was a slight increase in the total number of accidents, from 95,995 to 102,187, but this rise is held probably to be due to the fact that under the new road traffic act accidents must now be reported to the police, who thereby get to hear of more nonfatal accidents than in the past. Lieut. Col. J. A. A. Pickard, general secretary of the National Safety First Association, commenting on these facts, said that they were a source of great satisfaction to the association. They proved that the pessimists were wrong who prophesied that the passing of the road traffic act and the abolition of the speed limit would result in twice as many people being killed on the roads. The figures confirmed the association's observations that not only were automobile drivers generally showing more consideration to other road users but pedestrians were doing their share by being more alert and careful. Much of the credit was due to the local safety first councils, of which there were now nearly fifty.

Another Gigantic Nursing Home

Arrangements are made for the erection of a nursing home in the Marylebone Road, the consulting quarter of London, with 600 beds for patients, and hotel accommodations for relatives and friends, at a cost of $5,000,000. It is proposed to erect a building of nine stories, containing full facilities for all varieties of spa, electrical and other medical treatments, which will be available both for residents and for outpatients. It is anticipated that it will be possible to limit the charges of the nursing home to $5 a night and to reduce considerably the charges for many varieties of medical treatment. At present it is only in the hospitals that such facilities exist for medical treatment, and as a rule these are not used by the well-to-do. The latter are nursed in their own homes or in the small nursing homes, of which the facilities are very limited. The plan includes lounges of the hotel type, a roof garden laid out to give the greatest possible amount of sun and shelter, a pump room where every variety of medicinal water will be available, and a gymnasium for therapeutic purposes. It is intended to extend the scheme to Liverpool, Manchester and other large cities.

Award to Dr. W. B. Cannon

The Baly medal of the Royal College of Physicians is awarded every alternate year to the person who is deemed to have most distinguished himself in the science of physiology, especially during the two years immediately preceding. It has been awarded to Dr. W. B. Cannon, professor of physiology at Harvard. In presenting it, the president, Lord Dawson, described Dr. Cannon's contributions to knowledge as a monument of industry and achievement. Since Dr. Cannon took his M.A. degree in 1897, scarcely a year has passed that has not shown a harvest from his labors. Lord Dawson therefore could refer only to such pieces of his work as appeared to be landmarks. His first period, 1898-1910, was concerned with the experimental study of the movements and digestive activities of the alimentary tract, by means of the roentgen rays after opaque substances had been swallowed or injected. This work had recast our knowledge of digestion. In his second period, Cannon passed to the study of the effect of emotional states on gastro-intestinal function and thence to the physiology of the suprarenals—the association between epinephrine and fear, anger and hunger. Then came the war, and he worked in a casualty clearing station on the British front and later with General Finney of the U. S. Army at Dijon. Since the war he had been engaged in research into the function of the sympathetic, including the part played by it in the internal secretions.

In reply Dr. Cannon said that, over and over again, researches carried out in one direction proved by accident to be fruitful in another, and this had happened to him. The director of a scientific institution should always remember that the stimulus to work and the active cooperation received from students and collaborators must be taken into account when an individual is selected for personal award.

ITALY

(From Our Regular Correspondent)

Sept. 30, 1931.

The National Congress of Pediatrics

The Società italiana di pediatria held recently its fourteenth national congress at Florence, under the chairmanship of Prof. G. B. Allaria, director of the Clinica pediatrica of the University of Turin, aided by numerous foreign pediatricians. The session was opened in the Great Hall of the University with an address by Professor Allaria, who described the work of the Società di pediatria, which was founded in Turin in 1898 and which recently established also regional chapters. The speaker emphasized that the activity of the pediatric clinics is always directed toward ends that make for an improved national life. He explained also the proposal that the training of practicing physicians in pediatrics be made more comprehensive; furthermore, that health officers be required to take suitable courses in pediatrics, with the financial aid of the communes. The courses should be given at regular intervals and should take into account the fact that the professional activity of the health officer is devoted in large part to the prevention and treatment of diseases of children. Professor Allaria recalled the wonderful service rendered, in the field of pediatrics, by such great national organizations as the Opera nazionale per la protezione della maternità e dell'infanzia, the Red Cross, the Consiglio delle ricerche, and the Società di ortopedia, radiologia, eugenica e talassoterapia.

Addresses were delivered also by Professor Lereboullet, of the Academy of Paris, and Professor Mouriquand, of the Academy of Lyons.

Prof. Francesco Valagussa, subcommissioner of the Opera pro maternità e infanzia, reported that the society during the past three years expended 106,000,000 lire, or more than $5,000,000, in aid of mothers; 178,000,000 lire, or more than $9,000,000, in aid of children, and 24,000,000 lire, or $1,200,000, for the education in hygiene of the people of the rural districts. The results secured were as follows: In the ambulatoriums of the society, 88,442 mothers and prospective mothers, and 304,448 infants and children, were treated; fifty-nine ambulant chairs were created for maternal aid and puericulture, with 2,138 consultants, in which 88,095 mothers and gravidas and 1,800,000 children received aid. Aid was given during the nursing period to 77,000 legitimate mothers and to 27,000 unmarried mothers who recognized their obligations to their child. Prophylactic treatment in threatened tuberculosis was given to 23,000 children, and 6,000 were admitted to institutions as curable patients and as educable though abnormal. The hygienic conditions of 2,800 institutes were improved as a result of 3,141 sanitary inspections. By means of special legislative provisions, the society has brought it about that nearly all illegitimate children are at present recognized and fed at the breast. The number of such children recognized increased from 4,800 in 1927 to 27,580 in 1930. The society appointed a commission, with Prof. Filippo Bottazzi of Naples as chairman, for the study of alimentation in the institutes that receive children. The commission, to which works on pediatric subjects were contributed by physiologists, pediatricians and obstetricians, compiled dietetic tables that will be used in all the institutes. Just recently, the society established in Rome an aid center for mothers and children, which comprises ambulatoriums for nurslings, quarters for the admission and treatment of infants, quarters for the temporary admission of weakly children of an abnormal constitutional type, laboratories, rooms for roentgenologic and light treatment, and an experimental kitchen. The department for children is now complete, and the department for mothers is nearing completion and will begin to function in a few days. The work of the ambulant chairs for maternal aid and for puericulture is in full swing. They assist the mothers by training them in their duties, and apply to the nurslings the acquirements of puericulture and pediatrics. As a result, the morbidity and mortality in the rural districts have been greatly reduced. After Professor Valagussa's speech, the official topics on the program were taken up.

PURULENT PLEURITIS IN CHILDREN

The first topic, "Purulent Pleuritis in Children," was entrusted to four essayists. Professor Nasso, of the University of Messina, mentioned the various diseases, and most important of all, bronchopulmonitis, that give rise to purulent pleuritis. He considered the general and the local symptoms, which vary with the age and the condition of the patients, and explained the various clinical forms that pleuritis may assume in children. He discussed the various methods of clinical and etiologic classification, and described the course, the outcome and the possible complications of the disease. The speaker spoke finally of the differential diagnosis and of the prognosis, emphasizing that it is necessary to bear in mind, among various other data, the age of the patient and the primary disease.

Professor Castronuovo of Messina discussed methods of radiologic research applicable for the diagnosis of empyema and showed their value in determining the various clinical forms of purulent pleuritis.

Professor Laurisch, of the University of Naples, discussed the pathogenesis and the pathologic anatomy of purulent pleuritis. On the basis of 840 personal cases observed in the Clinica pediatrica of Naples, he connected purulent pleuritis with inflammatory conditions of the lung. He referred to certain bacteriologic data pertaining to pus in the pleura, and to the physicochemical conceptions that, according to most recent theories, regulate the formation of pus.

Professor Cocchi of Florence discussed the various methods of treatment for empyema. He demonstrated that better results are secured with medical treatment. He explained the method he used in about fifty cases, by means of which he succeeded in lowering the mortality to about 6 per cent.

In the discussion, Professor Lereboullet of Paris pointed out that in nurslings pleuritis is often associated with bronchopulmonary lesions, and that it is not exceptional to find it accompanied by pulmonary abscess. Professor Mouriquand of Lyons called attention to the importance of the symptom of dulness in the axillary region for the diagnosis of purulent pleuritis.

Professor Comba, director of the Clinica pediatrica in Florence, closed the discussion. Of the various methods discussed during the congress, the medical method appeared plainly the most advantageous, and only in a few special cases is surgical intervention justified. The physician should keep in mind all the methods proposed and apply in an individual case whichever promises to further the best interests of the patient.

ENCEPHALITIS IN CHILDREN

The second topic on the program, "The Syndromes of Encephalitis in Children," was introduced by Professor De Toni of Bologna, who explained the types of lesions encountered in various forms of encephalitis. The anatomic lesions are rarely characteristic, and hence an exact classification of the types of encephalitis, taking account of etiologic, anatomic and clinical criteria, has been impossible. With respect to the origin of the disease, a virus has been invoked concerning the existence and nature of which opinions are widely divergent.

Professor Taccone discussed the acute forms of encephalitis, observing that the diversity of the symptoms and the diverse mode of their development constitute clinical pictures so varied and inconstant that it is difficult to group them and describe them under separate and distinct headings. Nevertheless, Taccone sought to give a clear picture of the acute forms of encephalitis, not only of the primary disease but also of the types occurring secondary to infectious diseases and of the

epidemic forms. The prognosis depends on various factors, such as the age of the patient and the time of the development of complications involving the nervous system. The author spoke also of the treatment of encephalitis by means of injections of serum of convalescents.

Professor Bergamini of Parma considered the chronic forms of encephalitis and the sequels that occur in children. Also in these cases the subject is complicated by the difficulty of classifying forms of diverse symptomatology. The speaker explained both the psychic and the neurologic forms and emphasized that the prognosis of the chronic types of encephalitis must be very reserved, owing to the possible appearance of late and new symptoms.

Professor Midulla, delegate of the Opera Nazionale Balilla, explained the activities of the society that he represented, in addition to its educational work. He spoke of the service organized in the ambulatoriums and in the consultation centers, and of the adoption of the biotypologic record card, with which two million youths are now provided. He took up then the prophylactic work against social diseases and insurance against accidents, which have decreased in number in spite of the increase in the number of persons insured. The congress passed a resolution commending the activities of the Opera Balilla in the promotion of health and robustness of children and the human race.

Professor Galeazzi emphasized the need of collaboration on the part of pediatricians to organize a system of aid for lame, paralytic and mutilated children.

After the general discussion on encephalitis, the congress passed a resolution, presented by Professor Frontali of Padova, pertaining to the possible relations between vaccination against smallpox and the appearance of encephalitis. Since in recent years there has been developing, in medical circles and among the public, an exaggerated fear of smallpox vaccination, owing to the observation of cases of encephalitis following vaccination, the congress thought it advisable to announce that the vaccinal etiology is far from being demonstrated, and to urge that no changes be made in the laws and the practice of compulsory vaccination, which is the sole protection as yet known against epidemics of smallpox.

Professor Spolverini, director of the Clinica pediatrica in Rome, announced a new technic in artificial feeding. In spite of the fact that the best adapted food is used (cow's milk), and the most precise rules are followed, artificial feeding often gives results that are anything but satisfactory and commonly constitutes an ever present menace, especially in the institutes to which large numbers of nurslings are admitted. Studying the problem of cow's milk from the point of view of colloidal equilibrium, Spolverini and his co-workers succeeded, by means of the addition of a so-called colloid protector, in modifying the intimate structure of some constituents of cow's milk (particularly the casein), so as to bring about that certain phenomena of digestion (precipitation, coagulation and other processes) may be completed in almost the same manner as in the case of human milk. The colloid protector best adapted for the purpose has been found to be acacia. In applying this method for four years in his clinic, Spolverini has obtained very favorable results, aided by researches and laboratory examinations, and he expressed the hope that his colleagues might try the method and that they would confirm his observations.

DIETARY REGULATIONS FOR GROUPS OF CHILDREN

The last day of the congress was devoted to the elaboration of the topic "Dietary Regulations for Collective Groups of Children." The first speaker, Professor Macciotta of Cagliari, discussed the food requirements and the methods of determining them, emphasizing the importance of the surrounding conditions and of the constitutional status of the individual. He considered the alimentary value of the principal foods, pointing out that the most important source of vegetable proteins and carbohydrates lies in cereals. Professor Brusa of Milan spoke on alimentation in the first year of life and took up the diet of wetnurses. Professor Lucca of Turin explained the criteria to be followed in choosing the diet of older children up to the time of adolescence—criteria which vary according as it is a question of complete alimentation (continued stay in an institution) or partial alimentation (admission for part of the day), and dependent also on the age and the constitution of the person. The discussion was taken up by Professor Mouriquand of Lyons, Professor Bergamini of Parma, Dr. Capecchi, and others.

After a general discussion, the conventionists took a trip to Siena and then proceeded to Perugia, where the congress closed. Professor Allaria was chosen president of the society and Professor Valagussa was elected vice president. Rome was selected as the meeting place for the next congress.

International Congress of Surgery

At the ninth International Congress of Surgery, to be held at Madrid in 1932, the delegates from Italy will be Prof. Leonardo Dominici of Perugia, who will discuss "Diagnosis and Treatment of Intraspinal Tumors;" Professor Lusena of Genoa, who will consider "Surgery of the Esophagus," and Professor Uffreduzzi of Turin and Dr. Lorenzetti of Milan, who will describe "The Recent Advances in Surgical Anesthesia."

BERLIN

(From Our Regular Correspondent)

Nov. 2, 1931.

Modifications in Hospital Construction

The economic crisis has brought about marked retrenchments wherever it has been possible. In Berlin three hospitals have been closed entirely; in others, certain departments have been abolished. Nevertheless, in the opinion of many persons, there is need of a private hospital for the middle class, with moderate prices. Hence, in spite of the stress of the times, born of a certain courageous, optimistic spirit, a 100-bed hospital (landhausklinik) has been erected in Wilmersdorf (near Berlin) by the Vaterländischer Frauenverein, affiliated with the Red Cross Society. The new institution combines in a practical arrangement and with pleasing architectural features three functions in three partially separated buildings: the clinic, the aerztehaus and the nurses' pavilion. The aerztehaus, for the accommodation of the fifteen physicians on the staff, forms a right angle with the clinic building. At the apex of the angle are the entrances, the staircases, the elevators and the administration offices, so that, aside from the soundproofing, which was carried out with great care, all the essential noise-makers of the whole building are concentrated in one corner. The clinic comprises sixty rooms of uniform character, all provided with balconies toward the south and roll-back windows, in three parts, extending to the floor (for fresh-air treatment and the like). Perfect technic in the service of health is combined with comfort, which is accomplished through the shape of the rooms, the color scheme and the furnishings. The culinary department is managed by a well known restaurant chain, under medical supervision (an excellent innovation). For all the prescribed diets special menus are presented for the patient's choice, without the normal charges fixed by contract being exceeded. The clinic is managed from a caritative point of view on a non-profit-sharing basis and is thus not a private sanatorium in the ordinary sense; nor is it a hospital but is in a class by itself. In a period of social readjustment, which in its destructive phase is not yet completed, this institution is a good idea brought promptly to realization, which will bring aid and hence encouragement to the middle class, which is at present most endangered. At the same time the cost per bed, including the building costs for the clinic, nurses' pavilion and the aerztehaus with all its furnishings, was under $2,000.

Giessen, together with its university, has likewise accomplished wonders. In spite of the enormous difficulty in procuring funds, an orthopedic university clinic, which was urgently needed, has been supplied and has been recently opened. The clinic, which is under the directorship of Professor Pitzen, was built by the Hessischer Fürsorgeverein für Krüppel, which collected the money for the institution, one may say, a penny at a time, and placed it at the disposal of the university to be used for purposes of instruction and research. It has a sickroom section and a therapeutic section. The sickroom section is one-storied and is designed for seventy sickbeds, although there is enough space for a hundred beds, in case of need. The southern front of the sickrooms consists almost entirely of windows, all of which can be opened wide. The sickrooms are connected with the therapeutic section by a structure 21 meters long (likewise enclosed) which houses the medical baths and the gymnasium and serves at the same time as an auditorium. The gymnasium is connected by wide glass doors with a large campus, which is used for various athletic purposes. On the same plane as the sickrooms and the gymnasium is the first story of the therapeutic section, in which are the rooms of the administration, the policlinic, the x-ray room, the operating rooms, the workshops and the laboratory. The location of a portion of the workshops between the consultation room and the operating rooms is based on the desire to assure the absolutely necessary close connection between the physician and the orthopedic mechanics. All the rooms designed for patients lie on the same plane. The patients are not harassed by staircases, inclined planes or elevators. On the second floor of the therapeutic section are the rooms for the personnel, and in the basement are the culinary department, the heating equipment and further workshops. The total cost of the building was 350,000 marks ($83,300), or nearly $1,200 per sickroom.

Otto Warburg, Nobel Laureate

For his discoveries in regard to the nature and the mode of action of the respiration ferment, the Nobel prize in physiology and medicine, for this year, has been awarded to Otto Warburg, who is director of the Kaiser-Wilhelm-Institut for cell research in Dahlem (near Berlin), which was recently established for him by the Rockefeller Foundation. He is one of the most original investigators in the field of the chemical processes in the living cell. He was the first to demonstrate the decisive influence of the great surface development on the cell processes and studied out the biologic aspects of the notion of surface catalysis. He invented an exact precision method for the determination of the metabolism of the cells under various conditions—more particularly, of the oxygen intake of the cells, cell respiration and sugar decomposition in the cell without oxygen. Warburg opened up thereby a new outlook for the theory of cell metabolism and particularly of cell respiration.

Warburg's most important researches are in the field of the physiology of tumors and the mechanism of biologic oxidations. As for tumors, and especially the so-called cancer cells, he has demonstrated that these, in contradistinction to the normal body cells, are relatively independent of the available supply of oxygen; that is to say, that they have a metabolism without oxygen. Whereas normal animal cells die quickly in the absence of oxygen, the cancer cell can without oxygen continue to exist, to grow and to proliferate. Even when oxygen is available, it continues its oxygenless metabolism, the sugar decomposition, the same as yeast. Warburg developed from these observations a theory of the origin of tumors, in which there is certainly an element of truth. His contributions on the mechanism of cellular respiration are exceedingly important. He demonstrated that in every breathing cell there is a special oxidizing system—a respiration ferment, which activates the available oxygen material; that is to say, converts it into active oxygen. This respiration ferment he defined more precisely as an iron-containing organic dye, which closely resembles the hemin of the hemoglobin but is not identical with it. He was therefore the first to recognize with certainty the long suspected connection between iron in the cell and oxidative metabolism. The action of the respiration ferment is checked by hydrocyanic acid, so that the cell dies, which explains the exceedingly high toxicity of cyanogen compounds. He showed furthermore that iron also plays a part in the fermentation. More recently, he has announced the results of experiments that prepare the way for the harmonization of his respiration theory with the apparently entirely opposed theory of Heinrich Wieland of Munich, who was awarded, a few years ago, the Nobel prize in chemistry. Warburg is a theoretician and is a master of the chemical and the physicochemical method of research. He is an experimenter of the first rank and makes use of his mastery of method for his researches on the most difficult life processes.

VIENNA

(From Our Regular Correspondent)

Oct. 31, 1931.

Sudden Deaths of Eminent Physicians

During the past week, several eminent members of the medical profession in Vienna have died suddenly. First, Dr. Foramitti succumbed to a cerebral hemorrhage in a taxicab. He was the director of the Austrian ministry of health, also the Austrian delegate to the international health commission of the League of Nations, and the head of the hospital administration of our republic. His death, at the age of 58, is a great loss for the public health administration in our country.

The second death was that of Prof. Dr. Constantin Economo, the widely known investigator in neurology and brain research. This versatile scientist died in the midst of active service. He was the founder of the recently established laboratory for brain research in Vienna. In 1917 he became known throughout the world through his first published comprehensive description of epidemic encephalitis, which he observed in soldiers in the Vienna hospitals. His second important publication was an atlas of the cellular structure of the brain, in the form of 112 magnificent plates—a monumental work that required thirteen years (1912-1925) to complete. A second part, an atlas of the fibrous structure of the brain, had not been completed at the time of Economo's death. The deceased, an assistant of the Nobel laureate Professor v. Wagner-Jauregg, was asked to assume the directorship of the Klinik für Psychiatrie und Nervenkrankheiten, as the successor of his teacher; but he preferred to complete his researches on the brain, without being hampered by the duties of a clinical teacher. In connection with the organization of the first International Neurologic Congress of the postwar period, which was held in September of this year, Professor Economo, although in poor health, overexerted himself, which was possibly one reason for his unexpected death.

The third death was that of Dr. Arthur Schnitzler, the poet-physician. By his dramas and psychologic novelettes, significant through the intuitive feelings of the characters, and in which he anticipated the psychoanalytic researches of Freud, he was at an early age diverted from his medical practice; but in all his literary productions he gave abundant evidence of his medical training, especially as a psychoanalyst.

While this letter was being written, news came that the eminent roentgenologist Prof. Guido Holzknecht had died as a martyr and victim of his profession. He had suffered for years from carcinoma, which, some time ago, necessitated the amputation of several fingers of each hand. Six months ago,

his right arm had to be amputated. There developed, however, soon afterward a carcinosis of the skin of the thorax, with metastases in the abdomen, which hastened the end. Holzknecht was one of the first to recognize the significance of Roentgen's discovery for the progress of medicine. With his keen insight, he was able to separate the essential from the insignificant and to utilize it for research and diagnosis. Roentgen's discovery dates back to 1895. Six years later, Holzknecht published his "Atlas der Erkrankungen des Thorax," which gives evidence of his genius and his almost prophetic insight. Soon afterward he published his articles on "The Roentgenologic Diagnosis of Disorders of the Digestive Apparatus." Of great importance was his construction of the dosimeter for the measurement of the dosage of roentgen rays, which made possible the general use of the rays for therapeutic purposes and is known everywhere as the H instrument. This great medical achievement goes back to 1902. The Holzknecht unit is still employed. Holzknecht's importance as a creative guide was soon recognized, and, in spite of bureaucratic obstructionists, he succeeded in organizing the Central-Röntgen-Institut in the Vienna General Hospital and to make it one of the greatest institutes of the kind. Here a Holzknecht "school" developed, from which countless promising pupils have gone forth to occupy prominent positions in all parts of the world. From here have gone out the methods for the location of foreign bodies (projectiles), and the diagnosis of gastric cancer, kidney stones and cranial disorders. Holzknecht's fame was greater abroad than at home. He was generally regarded as the leading figure in roentgenology, and his work on roentgen injuries is a classic. The tragedy of his life was that he was doomed to die from such injuries. Thirty years ago, before he had invented his dosimeter, he observed in himself the first signs of roentgen "burns." His long-drawn-out illness did not, however, prevent him from continuing his research.

Inaugural Lecture of Prof. Dr. Denk on Cancer

Dr. Denk, the newly appointed professor for the first chair of surgery at the University of Vienna and the successor of Professor Hochenegg, began his lectures with a comprehensive inaugural address, delivered before a large audience composed of professors and students, on "The Modern Methods of Combating Cancer." After paying respect to his predecessor, he emphasized that his predecessor's chief care was the study of neoplasms. Continuing this tradition of the Vienna "school," he stated that he would likewise regard the combating of cancer as a most important need, in order that the continuity of the work of Professor Hochenegg might not be interrupted. The chief needs looking toward the cure of cancer are early diagnosis and early operation, the combating of recurrences, and the detection of persons who are threatened with cancer. To this category belong patients with precancerous disorders, subjects with hereditary tendencies to cancer, twins one of whom has already developed cancer, and the like. Periodic examinations with a view to prophylaxis are quite in order, which imposes an important rôle on the family physician, especially if it should prove possible to perfect the tests for cancer that are now available. In Graz (Styria), where Professor Denk has served as director of the clinic, he made use of the existing welfare services and applied control tests to persons operated on, thereby building up an organization that achieved favorable results. Periodic health examinations may become valuable as a means of promoting early diagnosis and treatment. On the other hand, postoperative supervision by welfare workers is an important measure to combat recurrences in season. Dr. Denk elaborated in Graz many new operative methods, which have made the operation on cancer much easier and more effective. Likewise radium treatment will contribute in great measure to an improvement in the operative results. With reference to the bloodless methods, the clinic must carry out just as careful researches, which (for the time being, at least) should be based chiefly on animal experimentation and on observations and use as postoperative treatment. In any event, Professor Denk expects from these researches, especially from the prophylactic side, great progress. A center for the detection of all cancer patients in Vienna is, in his opinion, an absolute necessity, in order to detect early recurrences, which should be treated, for the most part, by bloodless methods; but without the cooperation of the general practitioners such supervision would be impossible.

TURKEY

(From Our Regular Correspondent)

Ankara, Oct. 21, 1931.

Fourth National Medical Congress

The fourth biennial national medical congress recently convened in Ankara and was attended by more than 400 physicians from all over the country. Following the opening address, in which Ismet Pasha, prime minister, referred to the reports on nutrition as important subjects for discussion, Prof. Dr. Refik, minister of health and social assistance, who presided, addressed the congress. Prof. Dr. Server Kamil of the medical faculty of the department of hygiene reported on nutrition in cities, and Dr. Zeki Nassir on investigations into the question of nutrition in urban and rural communities. Prof. Dr. Kadri Rashit Pasha of the department of pediatrics discussed infant feeding, and Dr. Hamit Osman spoke on nutrition of the preschool child and of children of school age. Dr. Ali Shukri read a paper on the pathogeny, prevention, treatment and incidence of rickets in Turkey and Dr. Murat Ibrahim on the orthopedic and surgical treatment of rickets.

NUTRITION AND DIET IN TURKEY

In the report on nutrition and diet in cities in Turkey, Dr. Server Kamil suggests the establishment of cooperative agencies by means of which a good food supply may be insured at low cost. He recommends also that organizations concerned with the establishment of soup kitchens for the poor broaden their activities, that food inspection in cities be more severe, that food prices be standardized, and the public be educated in matters of food and nutrition and that, in particular, the bread, meat, milk and water supply of cities receive more attention. Owing to the scarcity of fresh milk, the import of all brands of evaporated, powdered and condensed milk is growing from year to year. He stated that pasteurized milk is not even in Istanbul available to the public and that the per capita consumption of milk in that city is 42 Gm. a day.

The report on the investigation into the question of nutrition in urban and rural communities revealed that from 70 to 90 per cent of the diet of the rural population in Turkey is of vegetable origin, and that the chief nourishment of the peasant is "bulgur," whole wheat which has been soaked previous to boiling and is then dried in the sun and coarsely pounded on a hollow stone. This serves for the preparation of soups and pilav. Country bread is made of wheat, rye, millet, barley and corn mixtures, from which, owing to the use of primitive implements, the bran has not been removed. An important fact is that the intake of animal protein of the rural population is most inadequate and that only mutton is used and no pork whatever; the latter is on sale only in large cities, such as Istanbul and Izmir. The peasant as a rule partakes of meat on rare occasions, only such as the Bairam days, the sacrifice offered being a lamb; or on the occasion of the celebration of a wedding party, or in case of an accident that makes it necessary to kill an animal. The demand for eggs in cities causes eggs to be more and more a luxury among the rural population; eggs in villages are as a rule now served only to guests. Butter,

so important an article of diet though solely a country product, is also, for economic reasons, rarely consumed by the producer. A considerable part of the rural population, especially in eastern and central Anatolia, does not know how to grow green leafy vegetables but includes in the diet raw onions, tomatoes, garlic, wild grasses and herbs, the knowledge of which has been handed down to them by their forefathers. Of fruits the peasant eats only those which grow in his particular village; the largest proportion is sold raw or dried. The antiscorbutic lemon is something never used in the peasant household.

What the peasant brings home in his bag from the city is sugar, salt, tea and coffee, which he values highly. Almost every peasant family owns a cow, a goat or a sheep. The rural population, however, does not drink milk, as it is turned into butter for sale, but of sour milk, or yoghurt, ample use is made in the diet. Sugar, a precious article, is seldom used for sweetening foods; as an addition to bread, honey or "pekmez," a nonfermented preparation of grapes, is used. While rice occupies an important place in the preparation of the city diet, its use is rare in rural communities. The peasant engaged in farm work takes a heavy breakfast before sunrise, a light lunch in the field, and a heavy supper in his home after sunset. A great number of city people do not take any breakfast at all or only a light one, but they take a heavy lunch and supper.

According to the geographic and climatic conditions and those of transportation and prosperity, five distinct zones in relation to diet in rural communities become obvious: the Black Sea coast, western Anatolia, the Mediterranean and southern provinces, and those of eastern and of central Anatolia. As the geographic condition of the Black Sea coast does not permit of the growing of wheat, corn bread is used there almost exclusively, and the oil of hazelnuts is utilized for the preparation of foods. Olive oil is not used by the inhabitants of eastern, central and southern Anatolia, but in western Anatolia and especially in the Mediterranean provinces ample use is made of it as well as of cottonseed oil, and, in the region where opium is cultivated, poppy oil is given preference over any other fat. In central Anatolia, sesame oil is used. Arabian influence in dietary habits, such as the use of highly spiced food and of raw meat, is noticeable in the southern provinces, while in the eastern provinces Russian, Caucasian and Persian influence is noticeable.

Of the deficiency diseases, ophthalmia and beriberi seldom occur, though some cases of pellagra are known to have come under observation. Because of the absence of iodine in water and food, endemic goiter prevails in some regions; scurvy is rare, and, owing to plenty of sunshine almost the year round, the incidence of rickets in rural communities is small. In the light of the newer knowledge of nutrition, the dietary habits of the rural population, which constitutes three fourths of the whole population, are deplorable; the existing conditions are largely due to established habits, ignorance and poverty. Absence of cheap transportation plays a large factor in the great difference between the dietary habits of urban and of rural communities. The most important aspect in regard to the problem of nutrition in rural communities is that the state of affairs so affects the constitution of the rural population that each generation has a lowered resistance to disease and is particularly susceptible to tuberculosis.

Prof. Tevfik Salim Pasha suggested that, among growing children unable to get the required amount of food, the sport activities in schools should be restricted; that the institute of hygiene now nearing completion take a lead in the education of the public in matters of food and nutrition, and that diet kitchens in connection with hospitals be established. Dr. Fahreddin Kerim stated that, much to the detriment of the population, alcohol had lately found its way into rural communities. Dr. Abdulkadir Lutfi recalled the deficiency diseases in the army during the World War and stated that today the conditions in relation to proper food were satisfactory. Dr. Ali Shukri reports that the difference in the incidence of rickets in urban communities (from 20 to 30 per cent) and in rural communities (from 5 to 10 per cent) is probably due to the fact that, winter and summer, the country children are out in the open almost all day.

Communications were read on such subjects as calcium metabolism, rickets and roentgen treatment, foreign bodies in the stomach, treatment of tuberculosis by artificial pneumothorax, lymphogranuloma, kidney stones, surgical treatment of stomach ulcers, the malaria campaign in Turkey, encephalitis following vaccination for scarlet fever, combined scarlet fever and diphtheria vaccine, simultaneous bilateral artificial pneumothorax, blood groups, new surgical treatment for old dislocations of the hip joint, hookworm eradication, ringworm in Turkey, food poisoning through Gärtner's bacillus, thymus tumors, suicides in Turkey, treatment of tetanus by suboccipital injection, treatment of diphtheria, thoracic and abdominal measurements in relation to the general development of infants, hemorrhage of the brain due to blackwater fever and to malaria, the method of early diagnosis in tuberculosis of the lung, and the Friedman vaccine.

A tea given at the model farm of the Turkish president marked the close of the three days of the congress. Prof. Dr. Refik, minister of health, was again asked to preside over the congress, at which intestinal parasites, amebic dysentery and mineral waters in Turkey will be discussed.

BUDAPEST

(From Our Regular Correspondent)

Oct. 31, 1931.

A Sign of Supermaturity of the Fetus

At a recent meeting of Hungarian gynecologists, Dr. Francis Szello read a paper entitled "A Sign of Supermaturity of the Fetus." He said that in his investigations he started with the physiologic fact that of the carpal bones the first to appear are the capitate and hamate; this is proved by the lime nucleus which is found at necropsies and by roentgenograms. These nuclei are never found in so-called mature infants born at the end of a regularly carried out gestation. They appear at the earliest in the second half of the first month of extra-uterine life, and at the latest in the sixth month. From this, he concludes that if, at the time of birth, both or one of these nuclei is present, the fetus is supermature. This is at present, he says, the only sure sign of supermaturity that can be easily shown on roentgenograms. If present, it is absolute proof, while its lack is not contradictory to supermaturity.

Harmful Effects of Iodine Injections Given as Abortifacients

According to Prof. J. Frigyessi, the rapid increase in the number of criminal abortions and the inflammatory diseases which they cause plays an important part in the great number of cases of sterility and extra-uterine pregnancy observed in late years. In one group of cases he blamed the action of intra-uterine iodine injections, used for provoking abortion. At the meeting of the medical society he reported two cases, in both of which violent cramps followed iodine injections; subsequently sterility, lasting for years, and finally extra-uterine gravidity resulted. In both cases he found knots, the size of a bean, in the uterine end of the tubes; the histologic preparations which he demonstrated showed in both cases a circumscript adhesion of the mucous membrane folds of the tubes, caused by the caustic action of tincture of iodine. The treatment consists in the excision of the knots and the restitution of the continuity of the tube by its implanation. But more important is the prophylaxis by the avoidance of intra-uterine iodine injections.

Marriages

ROBERT HARDIN HACKLER, JR., Asheville, N. C., to Miss Harriet Gresham Bates of Richmond, Va., November 20.

MAC M. DICKMAN, New York, to Miss Dorothy Kaufman of Westmount, Montreal, Que., Canada, October 11.

ALBERT WELKER COLLINS, Anderson, Ind., to Mrs. Janet McKenzie Dovey of Ottawa, Ill., November 14.

WALTER ORTHNER, Huntingdon, Pa., to Miss Lee Katherine Strohacker of Philadelphia, October 31.

RUFUS PRESTON SYKES, Asheboro, N. C., to Miss Blanche Lentz of Winston-Salem, November 7.

ELAM A. DRUM to Miss Mattie Elizabeth Walker, both of Richmond, Va., October 24.

HERBERT C. SCHLOSSER to Miss Lucille Short, both of Elkhart, Ind., November 14.

FRANK VICTOR THEIS to Miss Hazel Ericsson, both of Chicago, December 9.

JOSEPH COATES, Galax, Va., to Miss Ada Lee Cannaday of Pulaski, October 30.

Deaths

Charles Edward Dowman ● Atlanta, Ga.; Johns Hopkins University School of Medicine, Baltimore, 1905; member of the Southern Surgical Association, Associated Anesthetists of the United States and Canada, American College of Surgeons, Society of Neurological Surgeons, American Neurological Association and the Association for Research in Nervous and Mental Diseases; professor of pathology, Birmingham Medical College, 1911-1913; associate in surgery, University of Alabama, 1913-1915; instructor, associate and assistant professor of surgery, Emory University School of Medicine, Atlanta, 1915-1924; served during the World War; neurologic surgeon to the Scottish Rite Hospital for Crippled Children, Grad Memorial Hospital, Georgia Baptist Hospital, Piedmont Hospital and the Henrietta Egleston Hospital for Children; aged 49; died, November 14.

Walter Aikman Sherwood ● Brooklyn; Columbia University College of Physicians and Surgeons, New York, 1896; member of the American Surgical Association and the American College of Surgeons; served during the World War; aged 55; consulting surgeon to the Methodist Episcopal Hospital, Brooklyn, and the Eastern Long Island Hospital, Greenport; director of the department of surgery, Brooklyn Hospital, where he died, November 21, following an operation for appendicitis.

William Columbus Cox, Everett, Wash.; Jefferson Medical College of Philadelphia, 1885; member and past president of the Washington State Medical Association; member of the American College of Surgeons; member of the state board of medical examiners, 1900-1903; formerly mayor of Everett; honorary president of the staff of the General Hospital of Everett; aged 73; died, September 25.

Albert Ellis Douglas ● Nashville, Tenn.; University of Tennessee Medical Department, Nashville, 1892; member of the American Psychiatric Association; proprietor of a sanatorium bearing his name; formerly superintendent of the Central State Hospital; aged 65; died, November 15, in Oklahoma City, of pneumonia following an operation.

Ulysses Grant Souder ● Auburn, Ind.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; aged 65; medical superintendent of the Dr. Bonnell M. Souder Hospital, where he died, November 24, of Vincent's angina, pneumonia and acute lymphatic leukemia.

Summerfield J. Miller ● Madera, Pa.; Medical Department of the University of the City of New York, 1886; state senator, 1914-1922; formerly bank president; aged 72; died, November 10, in the Mercy Hospital, Altoona following an operation for hypertrophy of the prostate and myocarditis.

Herbert Thomas Penny, Cliftondale, Mass.; Central College of Physicians and Surgeons, Indianapolis, 1889; Columbian University Medical Department, Washington, D. C., 1896; member of the Massachusetts Medical Society; aged 68; died, November 19, of coronary occlusion and arteriosclerosis.

William Judson Lamson ● Summit, N. J.; Columbia University College of Physicians and Surgeons, New York, 1896; medical superintendent of the schools in Summit; aged 60; on the staff of the Overlook Hospital, where he died, November 28, of perforated ulcer of the duodenum.

Max Beegel, New York; Columbia University College of Physicians and Surgeons, New York, 1908; member of the Medical Society of the State of New York; on the staffs of the Jewish Memorial Hospital and the Gouverneur Hospital; aged 45; died, November 24.

William Lee Samuels ● Reno, Nev.; University of Louisville (Ky.) School of Medicine, 1897; past president and secretary of the Nevada State Medical Association; on the staff of St. Mary's Hospital; aged 57; died, November 1, of acute yellow atrophy of the liver.

Benjamin Richard White, Rochester, N. Y.; New York Homeopathic Medical College and Hospital, 1899; member of the Medical Society of the State of New York; on the staff of the Genesee Hospital; aged 55; died, November 13, of pneumonia.

Samuel P. Sesmer, Louisville, Ky.; Imperial Jurjev University, Russia, 1894; member of the Kentucky State Medical Association; aged 62; died, November 9, in the City Hospital, of chronic nephritis, uremia, bronchopneumonia and arteriosclerosis.

Ulysses Grant Poland ● Muncie, Ind.; Medical College of Indiana, Indianapolis, 1895; formerly city health officer and county coroner; on the staff of the Ball Memorial Hospital; aged 66; was found dead in bed, November 11, of heart disease.

Claude Addison Tallman, Maumee, Ohio; Northwestern University Medical School, Chicago, 1900; served during the World War; aged 53; died, November 21, in the Flower Hospital, Toledo, of injuries received in an automobile accident.

Geoffrey Joseph Fleming ● Ontario, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1898; member of the American College of Surgeons; aged 58; died, October 9, of pneumonia.

Eddie De Baun Thixtun, Gosport, Ind.; Central College of Physicians and Surgeons, Indianapolis, 1898; member of the Indiana State Medical Association; aged 63; died, November 21, in the Methodist Episcopal Hospital, Indianapolis.

John F. Shoemaker, St. Louis; Medico-Chirurgical College of Philadelphia, 1893; member of the Missouri State Medical Association, and the American Ophthalmological Society; aged 63; died, November 21, of cerebral hemorrhage.

Robert Woodworth Bell, Jr., Walla Walla, Wash.; Albany (N. Y.) Medical College, 1892; member of the Washington State Medical Association; connected with the U. S. Veterans' Bureau; aged 61; died, November 13.

James Ellis Brayshaw, Wilmington, Del.; Jefferson Medical College of Philadelphia, 1920; member and formerly secretary of the Medical Society of Delaware; aged 34; died, November 18, in the Homeopathic Hospital.

Claude Bertrand Cole ● Toledo, Ohio; Long Island College Hospital, Brooklyn, 1889; University of Pennsylvania School of Medicine, Philadelphia, 1893; aged 65; was found dead, November 22, of cerebral hemorrhage.

Samuel W. Latham, Eldorado, Ill.; St. Louis College of Physicians and Surgeons, 1901; formerly mayor of Eldorado and state senator; aged 53; died, November 1, of pneumonia, as the result of an injury received in a fall.

Charles W. Felix, Martwick, Ky.; University of Louisville School of Medicine, 1890; member of the Kentucky State Medical Association; died, November 18, in the Methodist Episcopal Deaconess Hospital, Louisville.

George Blythe Morris ● Goldsboro, N. C.; University of Maryland School of Medicine, Baltimore, 1910; aged 47; on the staff of the State Hospital at Goldsboro, where he died, November 15, of pulmonary tuberculosis.

Edwin Joseph Reeves, Princeton, N. J.; Tulane University of Louisiana Medical Department, New Orleans, 1893; member of the American College of Surgeons; aged 62; died, November 22, of endocarditis and arthritis.

Carlos M. White ● Visalia, Calif.; Rush Medical College, Chicago, 1901; past president of the Tulare County Medical Society; on the staff of the Kaweah Hospital; aged 59; died, in November, of arteriosclerosis.

John Richard Williams, Carrollton, Ohio; Bellevue Hospital Medical College, New York, 1881; formerly county coroner and member of the board of education; aged 73; died, November 23, of heart disease.

Frederick Barrett, Gilbert, Minn.; Rush Medical College, Chicago, 1897; served during the World War; for seventeen years mayor of Gilbert; aged 56; was found dead in bed, November 4, of heart disease.

Atlee Mairs, Charleston, W. Va.; Jefferson Medical College of Philadelphia, 1910; member of the West Virginia State Medical Association; aged 48; died, November 14, of a self-inflicted gunshot wound.

John T. Harris ● Tonawanda, N. Y.; University of Buffalo School of Medicine, 1883; for many years health officer and medical school inspector; aged 75; died, November 21, of coronary thrombosis.

Omar H. Tudor, Kenton, Ohio; Miami Medical College, Cincinnati, 1875; member of the Associated Anesthetists of the United States and Canada; aged 82; died, November 11, in the McKitrick Hospital.

Joseph Omer Guimond, Chicopee, Mass.; School of Medicine and Surgery of Montreal, Que., Canada, 1889; also a druggist; aged 71; died, November 8, in the New Haven (Conn.) Hospital.

Joseph B. Gallagher, Montreal, Que., Canada; McGill University Faculty of Medicine, Montreal, 1910; on the staff of the Montreal General Hospital; aged 47; died, November 25, of septicemia.

Wilbur Marchand Lilley ● Brownsville, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1899; aged 36; was found dead in bed, November 10, in California, of heart disease.

Albert Edward Mucklow, Brooklyn; Bellevue Hospital Medical College, New York, 1897; member of the Medical Society of the State of New York; aged 36; was found dead in November.

William Andrew Wilson, New York; St. Louis University School of Medicine, 1904; member of the American Urological Association; aged 32; died suddenly, November 28, of heart disease.

Carl Hattermann, Chicago; Rush Medical College, Chicago, 1886; member of the Illinois State Medical Society; aged 73; died, November 28, of lymphatic leukemia and gastric hemorrhage.

William Mason Green, Hastings, Neb.; Creighton University School of Medicine, Omaha, 1901; aged 36; died, November 8, in the Masonic Sanitarium, Bettendorf, Iowa, of carcinoma.

Willis Perry Woodard, Oak Park, Ill.; College of Physicians and Surgeons, Chicago, 1894; aged 72; died, November 22, of bronchopneumonia, cerebral hemorrhage and arteriosclerosis.

Edward C. Barstow, Washington, D. C.; Howard University School of Medicine, Washington, 1895; Spanish-American War veteran; aged 62; died, November 10, of heart disease.

Frank Arthur Zeller, Union City, Ind.; Ohio Medical University, Columbus, 1898; member of the Indiana State Medical Association; aged 61; died, November 14, in Visalia, Calif.

Edward W. Hawthorne, Gypsum, Kan.; University Medical College of Kansas City, Mo., 1894; member of the Kansas Medical Society; aged 77; died, November 17, of myocarditis.

Eugene H. Mohr, Alburtis, Pa.; Jefferson Medical College of Philadelphia, 1881; member of the Medical Society of the State of Pennsylvania; aged 74; died, November 12, of uremia.

William Loranzo Nuckolls, San Francisco; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; aged 65; died, September 25.

Charles Warren Weaver, Healdsburg, Calif.; Medical College of Ohio, Cincinnati, 1879; aged 77; died, September 10, in the Dante Sanatorium, San Francisco, of coronary thrombosis.

John C. McCandless, Chicago; Chicago Physio-Medical College, 1893; member of the Illinois State Medical Society; aged 66; died, November 30, of carcinoma of the bladder.

Daniel Brooks Stidworthy, Homer, Neb.; Sioux City (Iowa) College of Medicine, 1894; served during the World War; aged 65; died, November 14, of pernicious anemia.

John Thomas Wilson, Chicago; Meharry Medical College, Nashville, Tenn., 1895; aged 67; died, November 19, in the Dailey Hospital, of myocarditis and coronary sclerosis.

Edward Christian Rohrbach, Flat River, Mo.; American Medical College, St. Louis, 1908; aged 36; died, November 3, in St. Mary's Hospital, St. Louis, of sarcoma of the liver.

John George Moore Sloane, Holford, England; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1895; aged 58; died, August 24, of cerebral embolism.

Roy Ezra Sleppy ● Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1899; served during the World War; aged 36; died, November 10, of cardiac asthma.

Fred E. McKeeby, Olney Springs, Colo.; Medical Department of Omaha University, 1894; member of the Colorado State Medical Society; aged 61; died, November 12.

William Albert Lang, Long Beach, Calif.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1881; aged 67; died, September 9, of chronic myocarditis.

Joseph P. Dobbin, Quebec, Que., Canada; Laval University Faculty of Medicine, Quebec, 1902; on the staff of the Jeffrey Hale Hospital; aged 53; died, October 17.

Emil Gustave Reinert ● Hartford, Conn.; Baltimore Medical College, 1895; aged 65; died, November 21, in West Hartford, of carcinoma of the lip with metastasis.

Leonard E. Stocking, Agnew, Calif.; St. Louis Medical College, 1876; superintendent of the State Hospital; aged 81; died, October 29, of chronic myocarditis.

Thomas K. Wissinger, Columbus, Ohio; Starling Medical College, Columbus, 1879; aged 71; died, November 19, of arteriosclerosis and cerebral hemorrhage.

James Weir Heddens, Pasadena, Calif.; Jefferson Medical College of Philadelphia, 1879; aged 74; died, November 8, of arteriosclerosis and chronic myocarditis.

Arthur Montgomery Pelton, Los Angeles; University of Michigan Medical School, Ann Arbor, 1866; aged 87; died, September 7, following a prostatectomy.

Victor T. Roth ● Pottsville, Pa.; Medico-Chirurgical College of Philadelphia, 1891; aged 61; died, October 14, of cerebral hemorrhage and chronic nephritis.

William Laughlin Dunning, Newburgh, N. Y.; Bellevue Hospital Medical College, New York, 1892; aged 67; died, November 17, of cerebral hemorrhage.

William Boyd Secrest, Los Angeles; Ohio Medical University, Columbus, 1898; aged 62; died, November 2, of chronic myocarditis and coronary sclerosis.

John Willias Swetnam, Soldier, Kv.; Physio-Eclectic Medical College, Cincinnati, 1877; aged 80; died, October 5, of chronic interstitial nephritis.

Carl Henry Guess, Buffalo; University of Buffalo School of Medicine, 1880; aged 77; died, November 20, of diabetes mellitus and myocarditis.

Elbert D. Beckner, Hoxie, Kan.; University of Nashville (Tenn.) Medical Department, 1906; aged 53; died, October 20, of cerebral hemorrhage.

Robert Gideon Baxter, Caneyspring, Tenn.; University of Nashville Medical Department, 1885; aged 71; died in November of paralysis.

Henry Merrill Thompson, San Francisco; Jefferson Medical College of Philadelphia, 1906; aged 53; was found dead, October 20.

Leopold Gross ● New York; University and Bellevue Hospital Medical College, New York, 1910; aged 48; died, November 10.

Henry M. Beatty ● Trenton, N. J.; Jefferson Medical College of Philadelphia, 1885; aged 73; died, November 13, of heart disease.

George B. Roberts, Vanderbilt, Pa.; College of Physicians and Surgeons, Baltimore, 1886; aged 74; died, November 11, of nephritis.

James F. Brewer, Asheville, N. C.; Memphis (Tenn.) Hospital Medical College, 1899; aged 36; died, October 24, of myocarditis.

Payn Bigelow Parsons, New York; Albany Medical College, 1897; aged 59; was found dead, September 19, of heart disease.

Frank Charles Hood, Gold Run, Calif.; Hahnemann Medical College, San Francisco, 1884; aged 76; died, September 3.

Charles John Peirce, Los Angeles; Dartmouth Medical School, Hanover, N. H., 1885; aged 73; died, September 21.

Mary Jane Bearby, San Jose, Calif.; Homeopathic Hospital College, Cleveland, 1872; aged 87; died, September 3.

Ira H. Rea, Harbert, Mich.; Harvey Medical College, Chicago, 1898; aged 74; died, November 28, of pneumonia.

Alexander W. Shaver, West Hamilton, Ont., Canada (licensed, Ontario, 1877); died, October 2.

George Cryer Parker, Fort Smith, Ark. (licensed, Arkansas, 1903); aged 72; died, September 19.

M. M. Tubb, McMinnville, Tenn. (licensed, Tennessee, 1889); aged 75; died, November 24.

Joseph C. Hooten, Ellerslie, Ga.; Atlanta Medical College, 1893; aged 60; died, September 25.

Bureau of Investigation

THE CONVERSE TREATMENT

A Columbus, Ohio, Concern That Sells an Alleged Epilepsy Cure

The Converse Company, which on its letterheads is described as "The Converse Treatment Company," operates from 30 Smith Place Avenue, Columbus, Ohio. The head of the concern is said to be one Herbert E. Sanderson who, if reports are to be believed, has been in the "patent medicine" business for about fifty years. Connected with Sanderson (according to the company's stationery) are Frank J. Dawson and Donald W. Dawson, with L. P. Jackson, M.D., as "Medical Referee."

Dr. Louis P. Jackson of Columbus, who has practiced at Delphoss and Van Wert, Ohio, was, according to the records, born in 1867 and holds a diploma from the Starling Medical College of Columbus for 1898. Dr. Jackson is not a member of his local medical society nor of the American Medical Association.

The Converse Treatment has been discussed in THE JOURNAL at different times, but the large number of inquiries received by the Bureau of Investigation from both laymen and physicians

A Liberal Offer of Free Prizes
Mrs. Eggworth's Famous Cook Book
Universal Self-pronouncing Dictionary
The Old Favorite Song Book
This Self-filling Fountain Pen
H. E. SANDERSON

Photographic reproduction (greatly reduced) of a two-page leaflet sent out by Sanderson of the Converse concern to officials of villages and small towns in an effort to obtain "sucker lists" of epileptics. The "mayor," "president of the city council," or "justice of the peace" to whom the leaflet is sent, is offered trivial bribes for the names of sufferers from epilepsy.

makes it desirable to bring again to the attention of the profession and the public the facts regarding this mail-order exploitation of epileptics.

In the days before the passage of the Food and Drugs Act, the Converse Treatment was known as the "Converse Cure," and was described as "The only positive cure known, adopted and recommended by the leading physicians of the country." This statement, being one hundred per cent false, is no longer made by the company, although the implications in the 1931 advertising are almost as false and misleading. In the early days, the Converse nostrum was put out from Mount Vernon, Ohio, by a Mrs. Converse, who was said to have "discovered" the "cure." Although the company has for years claimed—and still claims—that its nostrum has been used by hospitals, sanitariums and physicians, no names or addresses are given to make a check-up on such claims possible.

Since the concern has been under the control of Sanderson, "sucker lists" of epileptics have for many years been obtained by sending broadcast to officials in rural communities a printed circular offering a small dictionary, a fountain pen, a cook book or a song book, free to those who will send a given number of names of epilepsy victims.

Of course, no information is given by the Converse concern regarding the composition of its product. In a booklet sent out at the present time, the public is told:

> "The Converse Treatment is prepared of the purest and most carefully selected herbs and medicines in its component parts, and with scrupulous exactness. Its distinguishing characteristic is the employment of a certain herb. This herb is gathered at a distance for the Converse Company at a particular season of the year and prepared for use in its laboratory. The Converse Treatment avoids entirely the powerful drugs known as Opiates, so often given for this trouble and is free from Alcohol, Morphine, Opium, Cocaine, Chloral, Heroin, Eucaine, Chloroform, Cannabis Indica, Acetanilid, or any of their derivatives."

The implication plainly is that the Converse nostrum is essentially herbs. Listing drugs that a "patent medicine" does *not* contain is an old trick in the business.

In the same booklet from which the quotation given above is taken, it is stated that the Converse Treatment has never been advertised in newspapers or magazines, but that the demand has "come entirely from results attained." The facts are, of course, the demand has actually come from those victims of epilepsy who have received the plausible and misleading "literature" of the Converse Company and whose names have been given the concern by those who are willing to furnish the contact at the price of a fountain pen or cook book.

As long ago as 1912, the Converse Treatment was analyzed by the late Senator E. F. Ladd, when he was the aggressive Pure Food Commissioner of North Dakota. Professor Ladd's report showed that the essential drugs in the Converse Treatment were the bromides. In 1915, the A. M. A. Chemical Laboratory, at the request of the Bureau of Investigation, made a thorough analysis of the Converse Treatment and the findings confirmed the earlier analysis of the North Dakota chemists. The A. M. A. Chemical Laboratory reported that from its analysis, it was evident that those who took the Converse Treatment in the dosage recommended obtained bromides corresponding to 58 grains of potassium bromide daily.

The Converse Treatment, quite obviously, has all the limitations and dangers of a bromide mixture.

TRIPLE L MEDICINE COMPANY

The Postal Authorities Declare Thomas N. Walker's "Syphilis Cure" a Fraud

In this department of THE JOURNAL for September 19, this year, there was published a brief story on the issuance of a fraud order against the West Medicine Company and Western Medical Clinic, exploited in Colorado. It was brought out in this item that the West Medicine Company was established in 1893 by one Charles West, the father of Amos C. West, who, at the time of the issuance of the fraud order, was the owner. A Dr. George D. Hoschouer had also operated the business prior to the acquisition of the concern by Amos C. West. Hoschouer conducted the concern under the name of the Western Medical Clinic, but when Amos West took it over, the name was changed back to the West Medicine Comany. The concern was selling through the mails two preparations, known, respectively, as "909" and "Brigham Young Tablets," the former an alleged cure for syphilis and the latter an equally alleged cure for "lost manhood." Amos C. West, it was brought out by the federal authorities, had no medical training, but was, in fact, a chiropractor and a real-estate operator. On August 24, this year, the Postmaster General debarred the West Medicine Company and the Western Medical Clinic from the United States mails.

Now, the postal authorities have issued another fraud order directed against the Triple L. Medicine Company and one Thomas N. Walker of San Francisco, Calif. Walker, it seems, is a linotype operator and has conducted, as a side-line, a piece of mail-order quackery known as the Triple L. Medicine Company, operating the business from his residence. The man has no medical or pharmaceutical training. "Triple L," as Walker calls his nostrum, is the same product that was known as 909, sold by the West Medicine Company of Denver. When the Post Office authorities began investigating the Triple L. Medicine Company, Walker admitted that his Triple L was the old 909 "cure" for syphilis. Chemical analysis by the federal authorities of this alleged cure showed it to contain 3½ grains of gold and sodium chloride to the ounce. This combination, of course, has no value whatever in the treatment of syphilis, and in fact, if taken over a long period, may produce very serious effects on the user. As a result of the investigation, the Hon. Horace J. Donnelly, Solicitor for the Post Office Department, recommended to the Postmaster General that a fraud

order be issued against the Triple L Medicine Company and Thomas N. Walker, debarring these from the United States mails. Such an order was issued Dec. 3, 1931.

In this connection, it may be said that in May, 1929, the Bureau of Investigation of the American Medical Association received information from Dr. C. B. Pinkham, Secretary-Treasurer of the Board of Medical Examiners of the State of California, relative to the Triple L Medicine Company, which was, at that time, under investigation by the state authorities. It was brought out that associated with the Triple L Medicine Company, at that time, was one R. L. Stine, M.D., who, it was alleged, had formerly been connected with the Dean Pile Institute of San Francisco. When Stine was interviewed by the state authorities, he is said to have admitted that he did not know what were the ingredients of the Triple L Liquid, which he was advising patients to take.

Correspondence

DISTRIBUTION OF BROMIDES IN THE BODY

To the Editor:—Because of your interesting editorial on the distribution of bromides in the body (THE JOURNAL, October 17, p. 1152), I should like to call attention to an illustrative but apparently little known piece of work on this question. The work was published by Erik Wilén in the *Uppsala läkareförenings förhandlingar* **31**:373, 1926, and contains carefully performed bromide (Br^-) and chloride (Cl^-) analyses on different tissues from a man who died after having taken during three days a quantity of about 100 Gm. of sodium bromide. The death ensued about a week after the beginning of administration of the sodium bromide. Wilén calculates that about 50 per cent of the sodium bromide ingested remained in the body at the death. Like Toxopéus, he found the concentration of bromide (Br^-) in the brain as a whole less than in several other tissues; e. g., blood, lungs, heart, spleen. However, when different parts of the brain were examined separately, it turned out that the bromide concentration in the cortex cerebri was about twice as great as that in the basal nuclei, of the cerebellum and of the white substance. The bromide concentration in the cortex was indeed exceeded only by that in the blood. Wilén correlates these observations with the selective action of bromides on the cortex but points at the same time at the relatively great water content of the cortex as a conceivable, simple chemical explanation of its relative richness in bromide.

GUNNAR BLIX, Uppsala, Sweden.

TUBERCULOSIS AND FLORIDA

To the Editor:—This communication, while dealing more specifically with Florida, is applicable to other resort states and winter playgrounds.

It has come to the notice of physicians in Florida that a considerable number of persons with pulmonary tuberculosis of varying grades of involvement and activity are sent to this state during the winter months for the purpose of availing themselves of Florida's climate and sunshine. The reason for this is apparent. These patients want to get away from the cold and confining northern winters and want to enjoy an outdoor existence.

People have been educated to the value of sunshine; hence one of the alluring enticements is that they can take the "sun cure" on the beaches and enjoy the salubrious climate. The unfavorable feature of the expedition is that they are left to shift for themselves. If the home physician knows the value of controlled exercise and the danger of a break in the routine of living, the patient is asked to report to him by letter at certain intervals. In many cases no definite instructions are given, and the patient is told to "lie in the sun" and take plenty of milk and eggs.

The result is that the patient arrives and equips himself to enjoy the bathing beaches. He puts on a bathing suit and goes out to lie for a half hour or two hours on a sunny beach. This brings on a bad attack of sunburn with its attending fever and misery and perhaps a lighting up of a quiescent lesion. The patient may decide to take a car or bus trip to another part of the state—he wants to see Florida. He goes to an occasional night club or is a fairly regular attendant of the race tracks. His rest hours are forgotten. His regular retiring hours are a memory. In the spring he returns to his family physician with an extension of his lesion or perhaps a history of pulmonary hemorrhage, and the physician blames the Florida climate as being unsuitable for pulmonary tuberculosis.

If this patient had followed his routine of living as closely as when under the observation of his home physician, he would be more definitely benefited than if he had remained at home. Florida has a suitable climate for the treatment of tuberculosis, but no climate can overcome a regimen that would wear down a healthy man. Tuberculosis here as elsewhere must be treated rationally, and a person who has been under the guiding care of a physician at home should be supervised wherever he goes, whether it is Florida, California or Arizona. If physicians recommending Florida to their patients would insist that these patients put themselves under the care of a physician when they arrive, much benefit would be derived from such a sojourn away from home.

This communication is written primarily to the end that tuberculous patients be put under the supervision of physicians when they go to a winter resort and that the resort physician keep in professional communication with the medical adviser who recommended the trip.

W. A. CLAXTON, M.D., Jacksonville, Fla.
Tuberculosis Clinician, State Board of Health.

PURE AIR AND CLEAN STREETS EXHIBIT

To the Editor:—Lack of proper methods of street cleansing and of the removal of waste detracts from the appearance of the city and invites negligence on the part of the public. It carries in its trend more important consequences than unsightliness and the pollution of bay waters. The open garbage can is a feeding place for insects and rodents and thereby contributes indirectly to the transmission of many diseases of which flies, vermin and rats are carriers. Improper sweeping results in filling the air with dust, as does the practice of dumping ash cans into open carts. Other deleterious elements in the air one breathes in the city are the carbon monoxide from the exhaust of automobiles, the smoke and soot which come from the chimneys of buildings and from stacks of boats plying in the city waters, the mineral dust that comes from building operations and from the tearing up of streets, the cleaning of buildings by sand blasting, and other similar sources.

The New York Meteorological Bureau in New York City measures daily the amount of dust suspended in the air, and it was found that over the Central Park area, which is probably one of the most favored areas in the city, the amount of dust and soot suspended averaged 3.97 tons daily to the cubic mile of air, during 1930. On moist days this suspension creates a pall which deprives the city of much sunlight and, particularly, of ultraviolet rays. Aside from the injury to the eyes and to the air passages, which the impurities of the air create, the amount of economic loss caused, directly or indirectly, is considerable. According to the estimates made a great deal of coal and oil is being wasted by improper combustion, and the destruction of fabrics and household effects runs into hundreds of millions

Bureau of Venereal Diseases, U. S. Public Health Service. No published statement with regard to the percentage development of positive blood reactions in originally seronegative primary cases under the influence of treatment seems to be available. It is well known, however, that this shift to positive, as a form of progression, does occur, and precautions should be taken to recognize the situation early in the course of the treatment by taking several blood tests at intervals of a week after the initial negative reaction, on the basis of which treatment was begun. Patients in whom such positive reactions subsequently appear are to be regarded as having fully developed infections, and should not be treated by an abortive or short-cut technic.

2. The general in vitro antiseptic properties of the arsphenamines are known, including their spirillicidal action, to a certain extent. These drugs in solution are not sufficiently powerful bactericides to justify any reliance on their self sterilizing properties. In the light of experience with modern technic, the use of tap water for arsphenamine injection without previous sterilization can only be regarded as reprehensible.

ALBUMINURIA AND INSURANCE

To the Editor:—A few days ago I had occasion to examine a school boy in apparently perfect health and found a small trace of albumin. The boy was examined by his family physician, who did not confirm my test. However, a few days later I found the same condition present again, and the observation was confirmed by the laboratory. Microscopic analysis showed 4 white blood cells to the high power field, no red cells, no hyaline casts, some shreds and small waxy filaments. What is the condition present and what effect, if any, should it have on his insurability? Please omit name.

M.D., New York.

Answer.—The data submitted are insufficient to afford any definite deductions. Evidently the albuminuria is not constant. It would therefore be advisable to determine whether it is postural or orthostatic by examining the urine passed in the morning after a night's rest. The absence of albumin at this time and its appearance after the patient has been active would suggest this condition. Nephritis can hardly be considered here unless the child has recently had an acute infectious disease with a renal involvement. Nephrosis is associated with large quantities of albumin, waxy casts and doubly refractive lipoid bodies in the urine, while glomerular nephritis is associated with small amounts of albumin, red blood corpuscles and hyaline casts. The presence of a few white blood cells in the urine, if constant, would suggest the possibility of some irritative process in the genito-urinary tract. Repeated examinations of the urine and a careful physical examination should be made and a temperature record kept, as the possibility of a chronic renal lesion or even a calculus without any subjective symptoms must be considered.

Formerly the tendency for insurance companies has been to refuse insurance to applicants with albuminuria. Several companies realize that transient or orthostatic albuminuria need not necessarily interfere with life and health and are now insuring the applicant with little or no rating up of the premium.

ALLERGIC SWELLINGS

To the Editor:—I have a patient, a woman, aged 39, married, who has had swelling, stiffness and some pain in the metacarpophalangeal and first interphalangeal joints of both hands for the past seven or eight years. These symptoms are most marked early in the morning and tend to disappear during the day. They are much more pronounced for several days preceding her menstrual periods and during the time of menstruation. The condition is not severe enough to be disabling but is annoying. The cervix was amputated ten years ago. She had a miscarriage nine years ago. The menses are scanty (two days) with considerable pain on the first day. The general physical condition is essentially normal. There have been no other pregnancies. Could there be any relation between the menses and the rheumatoid condition? Please discuss this case as to etiology and treatment. Please omit name.

M.D., Alabama.

Answer.—From the description of the transitory character of the swelling, tending to disappear during the day, the trouble is probably not inflammatory, as would have been the case if it were a rheumatoid arthritis. Furthermore, a chronic arthritis of the type described would almost certainly have led to some permanent deformity and restricted movement of the joint. The history indicates, rather, an angioneurotic edema. This receives further support from the greater intensity of the symptoms at the menstrual period, when the average woman is more nervous. It would be interesting to know whether the patient or her immediate relatives suffered from any allergic disease, as urticaria, hay fever, asthma or migraine.

In regard to treatment, it might be wise to make some food skin tests and then withdraw from the diet those foods to which the patient is sensitive. This treatment is based on the assumption that the trouble is allergic.

LEVULOSE

To the Editor:—Referring to the editorial in The Journal, October 24, page 1230, entitled, "The Absorption of Levulose," improved processes of production of this sugar are mentioned. Could you send to me references to recent articles describing these new processes?

Veader Leonard, M.D., Baltimore.

Answer.—A semicommercial plant capable of producing 50 pounds (22.7 Kg.) of levulose a day has been in operation at Iowa State College, Ames, Iowa, during the past year, using the Jerusalem artichoke as the raw material because of its many good features from an agricultural point of view. By drying the artichokes, many advantages are obtained, including the operation of the plant throughout the year.

A continuous precipitation process has been developed, yielding granular lime levulate, which may be easily filtered and washed. The preparation of crystalline levulose in good yields has been accomplished at ordinary temperatures (15 C.) without the use of refrigeration.

The history of levulose up to the year 1923 has been summarized by Harding (*Sugar* **25**:406, 636, 1923). Later investigations have been published by Jackson, Silsbee and Proffitt (*Indust. & Engin. Chem.* **16**:1250, 1924; Scientific Paper 519, 614, Bureau of Standards, 1926). The latest review including the entire literature of the subject will be found in a paper by McGlumphy and Eichinger (*Indust. & Engin. Chem.* **23**:1202 [Nov.] 1931).

NEED OF PERSISTENCE IN TREATING CONGENITAL SYPHILIS

To the Editor:—A boy, aged 15 years, unusually strong and well built and apparently in perfect health was accidentally found a year ago to have a four plus Wassermann reaction. There are none of the usual signs of hereditary syphilis nor is there any history of acquired syphilis. No family history is obtainable, as the boy was adopted when a baby and nothing is known about his parents. I have known him since he was 4 years of age and he has had no sickness during that time except an attack of measles. For the past year he has received intensive antisyphilitic treatment by a competent physician, but he still has a positive Wassermann reaction. Would you advise further treatment? Please omit name.

M.D., California.

Answer.—Treatment should be continued as intensively and constantly as the health of the patient permits. Congenital syphilis yields slowly in most cases. A careful examination of the nervous system and the spinal fluid is indicated.

USE OF VIOSTEROL DURING PREGNANCY

To the Editor:—Please advise me whether administration of irradiated ergosterol to pregnant women could cause a premature calcification of the fetal head, resulting in dystocia, with possibly damage later to the child.

Hallie Earle, M.D., Waco, Texas.

Answer.—There is no danger to mother or child from therapeutic doses of viosterol (irradiated ergosterol) given during pregnancy. In fact, such medication probably would be of advantage, owing to the excessive drain of calcium and phosphorus that takes place during this period. This medication is especially indicated in cases in which the intake of calcium compounds has been insufficient.

NONSURGICAL TREATMENT OF RECTAL PROLAPSE

To the Editor:—An elderly woman is suffering from a complete rectal prolapse of several years' duration. She refuses to have an operation. Can you suggest any measures or devices that would help to keep the prolapsed rectum in its normal position? Please omit name.

M.D., Wisconsin.

Answer.—There is no mechanical device known that will keep in place the prolapse of the rectum appearing in an old person. Careful attention to diet to give regular bowel movements; above all, avoidance of cathartics and, lastly, pressure on the prolapse with warm moist dressings after bowel movements, followed by light compression obtained by a T binder over the area, are the most important palliative measures.

HEART DISEASE FOLLOWING TRAUMA

To the Editor:—The answer in Queries and Minor Notes (The Journal, October 24, p. 1245) on "Heart Disease Following Blow Over Sternum" leads me to offer an additional reference; namely, Tuohy, E. L., and Boman, P. G.: Trauma to Viscera from Nonpenetrating External Injuries, with Special Reference to the Heart, *Ann. Int. Med.* **4**:1373 (May) 1931. These authors discuss three cases of auricular fibrillation following such trauma. One case was personally observed and the others were reported in two separate papers in the literature. This article is well worth reading for information on this little known subject.

William D. Reid, M.D., Boston.

Council on Medical Education and Hospitals

COMING EXAMINATIONS

ALABAMA: Montgomery, Jan. 11. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Clinical.* Chicago, Dec. 29. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

ARIZONA: Phoenix, Jan. 5-6. Sec., Dr. B. M. Berger, 12 North Central Ave., Phoenix.

COLORADO: Denver, Jan. 5. Sec., Dr. Wm. Whitridge Williams, 422 State Office Bldg., Denver.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, Dec. 29-30. *Regular.* Washington, Jan. 11. Sec., Dr. W. C. Fowler, District Bldg., Washington.

HAWAII: Honolulu, Jan. 11-14. Sec., Dr. James A. Morgan, Room 48, Young Bldg., Honolulu.

ILLINOIS: Chicago, Jan. 12-14. Supt., Mr. Paul B. Johnson, Springfield.

MINNESOTA: *Basic Science.* Minneapolis, Jan. 5-6. Sec., Dr. J. C. McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Regular.* Minneapolis, Jan. 19-21. Sec., Dr. E. J. Engberg, 524 Lowry Medical Arts Bldg., St. Paul.

NEBRASKA: *Basic Science.* Lincoln, Jan. 12-13. Act. Sec., Mr. P. H. Bartholomew, Lincoln.

NEVADA: *Reciprocity.* Carson City, Feb. 1. Sec., Dr. Edward E. Hamer, Carson City.

NEW YORK: Albany, Buffalo, New York, Syracuse, Feb. 1-4. Chief, Mr. Herbert J. Hamilton, Room 315, State Education Bldg., Albany.

NORTH DAKOTA: Grand Forks, Jan. 5-8. Sec., Dr. G. M. Williamson, Grand Forks.

OREGON: Portland, Jan. 5-7. Sec., Dr. C. J. McCusker, 1014 Medical Dental Bldg., Portland.

PENNSYLVANIA: Philadelphia, Jan. 5-9. Sec., Mr. Charles D. Koch, Harrisburg.

RHODE ISLAND: Providence, Jan. 7-8. Dir., Dr. Lester A. Round, 319 State Office Bldg., Providence.

SOUTH DAKOTA: The St. Charles Hotel, Pierre, Jan. 19-20. Dir., Dr. H. R. Kenaston, Bonesteel.

WASHINGTON: *Basic Science.* Seattle, Jan. 14-15. *Regular.* Seattle, Jan. 18-19. Dir., Mr. Charles Maybury, Olympia.

WISCONSIN: Madison, Jan. 12-14. Sec., Dr. Robert E. Flynn, 315 State Bank Bldg., LaCrosse.

WYOMING: Cheyenne, Feb. 1. Sec., Dr. W. H. Hassed, Capitol Bldg., Cheyenne.

Arizona October Examination

Dr. B. M. Berger, secretary, Arizona State Board of Medical Examiners, reports the written examination held at Phoenix, Oct. 6-7, 1931. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Fourteen candidates were examined, 12 of whom passed and two failed. The following colleges were represented:

PASSED	Year Grad.	Per Cent
College of Medical Evangelists	(1930)	80.8
Stanford University School of Medicine	(1929)	89
Northwestern University Medical School	(1930)	89.6
Rush Medical College	(1931)	85.8
University of Illinois College of Medicine	(1929)	86
Indiana University School of Medicine	(1930)	82
University of Louisville School of Medicine	(1930)	84.5
University of Maryland School of Medicine and College of Physicians and Surgeons	(1930)	88.5
Harvard University Medical School	(1929)	81.2
University of Minnesota Medical School	(1930)	80.2
University of Cincinnati College of Medicine	(1930)	80.8
University of Toronto Faculty of Medicine	(1931)	76.6

FAILED		Per Cent
Osteopaths	64.1,	64.4

North Carolina June Report

Dr. John W. MacConnell, secretary, North Carolina State Board of Medical Examiners, reports the written examination held at Raleigh, June 15, 1931. The examination covered 16 subjects and included 70 questions. An average of 80 per cent was required to pass. Seventy-four candidates were examined, all of whom passed. Fifteen physicians were licensed by endorsement of credentials. The following colleges were represented:

PASSED	Year Grad.	Per Cent
Howard University School of Medicine	(1930)	81, 88.6
Emory University School of Medicine	(1931)	86.3
University of Louisville School of Medicine	(1929) (1931)	82.3, 84.3, 92.4
Tulane University of Louisiana School of Medicine	(1930) (1931)	91.3, 93.4, 94
Johns Hopkins University School of Medicine	(1931)	86.4, 95
University of Maryland School of Medicine and College of Physicians and Surgeons	(1931)	84.4, 85.6, 86.4, 89.4
Harvard University Medical School	(1931)	94.3
Washington University School of Medicine	(1931)	87.7, 90.7
Syracuse University College of Medicine	(1930)	89.1
Jefferson Medical College of Philadelphia	(1931)	86.3, 86.4, 87.4, 88.9, 89.3, 90.3, 90.4, 90.7, 94.4, 95
Temple University School of Medicine	(1930)	89.4
University of Pennsylvania School of Medicine	(1928) (1931)	82, 83.7, 87.3, 87.6, 87.9, 88.1, 89.1, 89.3, 89.9, 90, 90.4, 90.4, 90.7, 91.4, 92.1, 93, 94.4
Medical College of the State of South Carolina	(1931)	82.1, 85.9, 89.6
Meharry Medical College	(1927) (1928)	80, 83.3, (1930) 80, 89.4
Baylor University College of Medicine	(1919)	84.1
Medical College of Virginia	(1930)	85.1, 89.3, (1931) 83.4, 83.4, 85.9, 86.1, 86.3, 87, 87.3, 87.3, 87.7, 88, 88.3, 88.4, 88.9, 89, 89.4, 91
University of Virginia Department of Medicine	(1928)	92.7

LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Emory University School of Medicine	(1923)	Georgia
University of Georgia Medical Department	(1928)	Georgia
Rush Medical College	(1929)	Illinois
Baltimore Medical College	(1893)	New York
Johns Hopkins University School of Medicine	(1925)	Virginia
University of Maryland School of Medicine	(1908), (1914)	S. Carolina
Harvard University Medical School	(1927)	N. B. M. Ex.
Bellevue Hospital Medical College, New York	(1891)	S. Carolina
University and Bellevue Hospital Medical College	(1920)	New York
University of Cincinnati College of Medicine	(1928)	Ohio
Jefferson Medical College of Philadelphia	(1922)	Virginia
University of Pennsylvania School of Medicine	(1917)	Penna.
Medical College of the State of South Carolina	(1928)	S. Carolina
Laval University Faculty of Medicine	(1927)	Canada

Book Notices

The Influence of Diet on Caries in Children's Teeth. [Interim Report]. By the Committee upon Dental Disease. Medical Research Council, Special Report Series, No. 159. Paper. Price, 6d. Pp. 19, with 3 illustrations. London: His Majesty's Stationery Office, 1931.

This is a progress report of observations, extending over a period of about two years, made on 332 children receiving institutional care in and near Birmingham. The children were housed in separate cottages, which was a factor of assistance in carrying out the plan of investigation followed. All the children of a given cottage received test substances as daily additions to their regular diet. The administration of these supplements was carefully supervised by the foster mother. The diet of institution I was supplemented daily by treacle (golden syrup), from 28 to 42 Gm. (1 to 1½ ounces), according to the age of the child. At institution II, olive oil, from 14 to 21 cc. (1 to 1½ tablespoonfuls), according to age, was given as the daily supplement; later a second group at this institution received a similar amount of a solution of viosterol in olive oil. At institution III a group of children received a daily supplement of cod liver oil, the amounts being the same as for the olive oil experiments. Careful dental inspections were made at intervals of six months; the present report deals only with the number of erupted teeth and the presence and extent of caries. The data are treated statistically in order to determine the significance of the observations noted. There was an increase in the incidence and extent of caries in all groups, but in the case of those groups receiving fat-soluble vitamins (cod liver oil and viosterol solution) the increase was only about one-third that in the other groups. There was no significant difference in the rate of increase of caries between the children receiving olive oil and those receiving treacle. "The facts indeed seem to warrant the conclusion that the incidence and rate of progress of caries in teeth, either fully or nearly fully calcified, can be considerably retarded by the addition of fat-soluble vitamins to the normal diet. The general similarity of the results obtained from the use of cod liver oil and radiostol, respectively, suggests strongly that the potent factor in securing this retardation is vitamin D, inasmuch as it is common to both substances."

The Penalty: Must We Pay It? By Dr. Abraham Strachstein. Cloth. Price, $1. Pp. 138, with illustrations. New York: Good Health Publishing Company, 1931.

This book is labeled "a frank discussion of the social disease problem written so that whoever reads will understand." It is not especially well written. The words "luetic" and "lues" are used instead of "syphilitic" and "syphilis." The volume will not be understood by the vast majority of uneducated persons, who constitute the chief problem in control of venereal disease. The word "preventative" is used instead of "preventive," and in general the book is not quite up to what such a book ought to be.

Malaria Investigations in Some Parts of the Transvaal and Zululand. By N. H. Swellengrebel, Professor of Parasitology, University of Amsterdam, Holland, S. Annecke, M.A., M.B., B.S., Medical Inspector (Malarial), Public Health Department, Union of South Africa, and B. De Meillon, M.Sc., F.E.S., Acting Entomologist, South African Institute for Medical Research, Johannesburg. Publications of the South African Institute for Medical Research. Volume IV, No. 27. Edited by the Director. Paper. Pp. 245-274, with 18 illustrations. Johannesburg: South African Institute for Medical Research, 1931.

The only mosquitoes found to be concerned in malaria transmission were Anopheles funestus, Anopheles costalis and Anopheles pretoriensis. The natural index of infection in each case was: funestus, 15.9 per cent (340 examined); costalis, 15.6 per cent (205 examined), and pretoriensis, 1.7 per cent (114 examined). The conditions were found to be favorable to species control of the incriminated anophelines. A. funestus breeds in streams with grass-covered banks, especially where the current is not strong; it prefers water that is clear and fresh. A. costalis is a puddle breeder, being found in the most temporary mud puddles which are lacking in vegetation and without shade. A. pretoriensis is thought to play little part in natural transmission, probably because of its lack of contact with man. Evidence is presented which indicates that human gamete carriers (of estivo-autumnal malaria) with infections as low as 1 gamete to 1,500 leukocytes may infect anophelines. The native population in highly malarious areas shows a resistance to the disease. This is demonstrated by the lack of obvious signs of suffering in young children with heavy infection; by an acquired immunity later on, as shown by reduction of the parasite rate and a high spleen rate; and among adults by an acquired tolerance, as shown by a lessened spleen rate and a continued state of immunity, so that the parasites are kept low in numbers.

Gynecology and Urology for Nurses. By Samuel S. Rosenfeld, M.D. F.A.C.S., Adjunct Obstetrician and Gynecologist, Lebanon Hospital, New York City. Cloth. Price, $2. Pp. 230, with 97 illustrations. New York: William Wood & Company, 1931.

Because of the close relationship between gynecology and urology, the author presents a brief picture of these subjects. He falls short of making it of great value by devoting too little space to the subject of the nurse's responsibility in these conditions, and actual nursing care. The final chapter, written on postoperative care, appears to be a set of rules for hospital routine such as may be seen posted in the house staff room in some institutions. Lacking in this chapter is any discussion of postoperative complications and instruction to the nurse on how to recognize and evaluate untoward symptoms and signs. The book could be made more useful by revision in subsequent editions.

Atlas der Röntgenstereoskopie. Von Dr. Max Cohn, dirigierender Arzt der Röntgenabteilung am Städt. Krankenhaus im Friedrichshain-Berlin. 1. Serie mit 20 Filmdianegativen und einem Betrachtungsapparat. Cloth. Price, 22 marks. Pp. 26. Leipzig: Georg Thieme, 1931.

This collection includes a text by Dr. Max Cohn, a folding stereoscope and twenty stereoscopic negatives of roentgen appearances. Such conditions as tuberculosis of the kidney, appendicitis, gallstones, carcinoma, ulcers, echinococcosis, fractures, tumors of the brain, and various types of cysts are illustrated.

Exploration radiologique de l'appareil respiratoire. Par Emile Bergeat, professeur à la Faculté de médecine de Paris, Francis Bordet et Henri Durand, chef du laboratoire de la clinique de la Charité. Avec la collaboration technique de J. Couvreux, chef du laboratoire de radiologie de la clinique de la Charité. Fascicule I et II. Cloth. Price, 350 francs per set. Pp. 465, with 639 illustrations. Paris: Masson & Cie, 1931.

This work is printed on excellent paper to bring out the roentgenographic illustrations to the best advantage. The scheme has been to publish the diagnosis and caption in close proximity to the illustration, to facilitate the intelligent study of the condition. The work is divided into three general parts: the first sets forth as briefly as possible the technical and roentgenologic exploration of the respiratory system, followed by general remarks on the value and interpretation of the results contributed to the clinical study by roentgenology. The second part is dedicated to the study of the basic principles, beginning with descriptions of the roentgenologic images of the normal respiratory tract. In the third part of the work there are described in order the roentgenologic appearances of the various respiratory disorders, classified under the following heads: thoracic cage, diaphragm, mediastinum, trachea and bronchi, pleura and the lungs. The text is adequate and not too brief. The captions contain the essential facts relating to each of the illustrations. The use of iodized oil in bronchiectasis is also described in detail, and certain other lesions are carefully described. This monumental work contains a veritable mine of information relating to the roentgenologic investigation of the respiratory tract.

Diseases of the Skin. By Richard L. Sutton, M.D., Sc.D., LL.D., Professor of Diseases of the Skin, University of Kansas School of Medicine. Eighth edition. Cloth. Price, $12. Pp. 1352, with 1301 illustrations. St. Louis: C. V. Mosby Company, 1931.

The first edition of Dr. Sutton's textbook appeared in 1916. The present edition includes a rearrangement of the illustrations, the use of a lighter and finer grade of paper, and much new material. The book is modern, and particularly safe as a guide for the general practitioner, since it does not offer to him technics involving roentgen or similar procedures suitable only for use by the specialist.

Die physikalische Seite des Blutgerinnungsproblems und ihre praktische Bedeutung. Von Dr. med. Heinrich Lampert, Privatdozent an der Universität Frankfurt a. M. Paper. Price, 10.50 marks. Pp. 127, with 45 illustrations. Leipzig: Georg Thieme, 1931.

This monograph presents results of studies of the physics of blood clotting. The function of surface forces in clotting receives especial attention. For blood transfusion, correct counting of thrombocytes and other purposes, it is desirable to use containers—syringes and vessels—the surfaces of which delay clotting. The author has made an effort to find substances that are more practical than paraffined glass for this purpose. Certain formaldehyde-phenol products delay coagulation, but the most promising substitute for paraffined glass appears to be amber, which, besides presenting surfaces which inhibit clotting for a time, also has the highly desirable quality of transparency. The author believes that his results will lead not only to valuable practical improvements in the handling of fresh blood but also to new and fruitful methods of investigating the blood itself.

Quantitative Estimation of Vitamin D by Radiography. By R. H. Bourdillon, H. M. Bruce, C. Fischmann and T. A. Webster. Medical Research Council, Special Report Series, No. 158. Paper. Price, 1s. Pp. 48, with illustrations. London: His Majesty's Stationery Office, 1931.

This is a detailed account of a method for the quantitative estimation of vitamin D, based on the roentgenographic examination of the healing of rickets in rats, for which an arbitrary scale of twelve different stages of healing is used. The curative effects of graded doses of the substance under examination are compared with the effects produced in a comparable series of animals by doses of a standard preparation, both being measured in terms of the roentgenographic scale described in this paper. Some of the factors taken account of in using this technic are breeding stock, age, weight, diet and caging of the young rats used for the test, and x-ray plant operated under specified conditions. A representative healing scale with detailed description is presented. Twelve roentgenograms comprise the series used in the scale, each picture being distinct enough to be distinguished from the others and to represent a definite state in the calcification process. The scale has been calibrated by tests on a large number of rats and found to be approximately logarithmic in nature. The chief sources of error in this technic prove to be variations in response of litter mates to vitamin, and mistaken judgment as to the degree of healing, the latter being responsible for nearly a third of the total error.

Bedside Interpretation of Laboratory Findings. By Michael G. Wohl, M.D., Associate Professor of Experimental Medicine, Temple University Medical School. With an introduction by Joseph McFarland, M.D., Sc.D., Professor of Pathology, University of Pennsylvania. Cloth. Price, $6. Pp. 521, with 133 illustrations. St. Louis: C. V. Mosby Company, 1931.

This book is noteworthy for its simplicity. It adds a few clinical interpretations of laboratory observations to those found in the ordinary textbooks on laboratory and clinical methods of diagnosis. In reality, the book is merely a summary of the work found in many textbooks and correlated for the purpose of clinical medicine and bedside teaching.

Medicolegal

Narcotic Addiction as Affecting Veracity

(Kelly v. Maryland Casualty Co. (U. S. D. C.), 45 Fed. (2d) 782; Maryland Casualty Co., Inc., v. Kelly (U. S. C. C. A.), 45 Fed. (2d) 783)

The Maryland Casualty Company, Inc., insured the Bank of Ivanhoe against loss by robbery or burglary. The bank was robbed. The plaintiff, J. M. Kelly, as receiver of the bank, thereafter sued the company, to recover under the insurance policy the amount lost through the robbery. In the United States district court for Western District of Virginia, Henry Clay McDowell, Judge, judgment was given in favor of the plaintiff, and the insurer thereupon appealed to the United States Circuit Court of Appeals, Fourth Circuit.

The cashier, a woman, was the principal witness for the plaintiff. She testified that while she was alone in the bank a masked man entered, pointed a pistol at her, and demanded the money in the bank. She handed him the money in the cash drawer, some $600 or $700, and then became unconscious. When she regained consciousness two hours later, she was locked in the vault, from which $5,600 was missing. She was in an hysterical condition and had hysterics and convulsions, which might have been either feigned or involuntary, from the time of her release from the vault until she was taken to the hospital about seven days later. On entering the hospital, she claimed to be suffering from an injury to the head, which she thought had been inflicted at the time of the robbery, either by a blow from the robber or by a fall. Her physician testified that during eighteen months he had personally administered to her from time to time, to relieve her from suffering, from 3 to 5 grains of morphine per week. The physician who saw her when she was admitted to the hospital testified that she was under the influence of morphine and was not suffering from a blow on the head. There was evidence that she had taken 4 grains of morphine and 5 ounces of chloroform the night before. There was, however, no evidence to show that she was under the influence of morphine either at the time of the alleged robbery or when she was testifying.

Counsel for the defendant insurance company, desiring to impair the credibility of the witness, offered to prove by a physician then present that she had for about eighteen months been addicted to the use of morphine. This physician, he said, would furthermore testify:

> My opinion is that an excessive use of morphine, such as indicated, might tend to undermine the morale of a person, especially for truthfulness, and make them cunning. It also tends to make them unreliable. I might also say that a drug addict might feign anything.

As the witness, the cashier of the robbed bank, had testified that her condition was due to her injuries, evidence of her addiction to the use of narcotic drugs, tending to contradict her testimony, was competent and admissible for that purpose. Such evidence was held incompetent and inadmissible, however, for the purpose of proving that the witness "was a dope addict, and that dope addicts are incredible."

In passing on the proffer of evidence to show that the witness was a narcotic addict and the effect of such addiction, Judge McDowell discussed elaborately and carefully the admissibility of evidence of narcotism, and more especially of evidence of morphinism, for the purpose of weakening the credibility of a witness. To that end he examined not only law books but every medical work that he was able to obtain from local physicians. In discussing this rather unusual resort to medical literature, Judge McDowell quoted Wigmore as follows:

> "Finally (and apart from the use, already referred to, of literary works and dictionaries) there is often found an open and deliberate citation by the court itself to encyclopedias, medical works, and the like, as giving a foundation of fact for subjects involved in their decisions."—3 Wigmore, Ev. (ed. 2), section 1700 d, page 651.

Several rules of law concerning the admissibility of evidence of drug addiction have been stated, said Judge McDowell, and,

> no court could have formulated, and no court could intelligently adopt or reject, any one of those rules, without having accepted as sound some theory as to the usual effect of narcotic drug addiction on the addict. And an intelligent adoption of one, rather than of some other, scientific theory makes necessary some knowledge of the different theories and of the reasoning supporting them. It seems to me to follow that it is the duty of a judge in my situation to inform himself as well as he reasonably may concerning the reasons for the differing medical opinions before he undertakes to make a choice between them.
>
> Again, it is to my mind much more satisfactory for the judge to read all the medical works he can reasonably obtain, rather than to rely wholly on the medical works selected by medical witnesses, whose selections might easily be influenced by conscious or unconscious partisanship.

Typical among the quotations from medical books, that Judge McDowell set forth to show what he found to be evidently, until recent times, the universal, or almost universal, medical opinion, and to be still the medical opinion of a very considerable body of writers, is the following:

> "Persons addicted to morphia are inveterate liars, and no reliance whatever can be placed upon their statements. In many instances this is not confined to matters relating to the vice."—William Osler and Thomas McRae, Principles and Practice of Medicine (ed. 9), p. 392.

Judge McDowell found, however, medical writers supporting "a more modern theory," and quotes effectively from what they have written. The following is typical of these quotations:

> "No addict who receives an adequate supply of opium and has money enough to live is converted into a liar or thief by the direct effect of the drug itself."—Lawrence Kolb, U. S. Public Health Service, Drug Addiction in Its Relation to Crime, Mental Hygiene 9: 74-89.
>
> "That individuals may take morphine or some other opiate for twenty years or more without showing intellectual or moral deterioration is a common experience of every physician who has studied the subject."—Lawrence Kolb, U. S. Public Health Service, Pleasure and Deterioration from Narcotic Addiction, Mental Hygiene 9: 699, 724.

In view of the conflicting statements in medical literature, Judge McDowell concluded:

> it is manifest that there is now no consensus of medical opinion to the effect that morphine addicts are usually abnormally untruthful in respect to matters not connected with the vice. And it follows that there is no justification for treating the older theory, or either theory, as a matter of common knowledge.

On the other hand, he found an agreement, practically universal, on two points:

> Nearly all drug addicts are untruthful in respect to the fact of addiction. This is also true in respect to obtaining, and in respect to retaining possession of, the desired drug, where there is any fear of a failure of supply.

On the whole, Judge McDowell concluded, an inference that morphinism usually causes abnormal mendacity in respect to matters in general is of such doubtful validity that it cannot be accepted as a matter of law.

The theory that narcotic addicts live in an unreal world and thus become unable to distinguish between images and facts, stated in *State* v. *Fong Loon*, 29 Idaho 248, 158 Pac. 233, and in Wharton and Stillé, Medical Jurisprudence (ed. 3), section 1111, Judge McDowell found himself unable to accept, arguing:

> But because a narcotic drug has some particular effect on people who are unaccustomed to such drug, it does not follow that the same drug has a similar effect on those who have become addicted to its use. . . . I cannot here do more than say that the impression left on my mind by the medical works I have read is that morphine addicts obtain from their usual dose merely freedom from "withdrawal pains," and that pleasurable sensations, including the dream state, can be obtained only occasionally and by means of a sudden increase in the size of the dose.
>
> At the least, there is certainly room for some doubt if narcotic drug addicts do live in an unreal world. And, even if they do, the assertion that long-continued day dreaming causes mendacity seems to me to require more supporting evidence than I have been able to find. Day dreamers are usually impractical people, but they are not generally understood to be more untruthful than are people who do not indulge in day dreaming.

The rule laid down in the Cyclopedia of Law and Procedure (40 Cyc. 2575) which authorizes the introduction of evidence to show that a narcotic drug addict was under the influence of the drug of addiction at the time of the occurrence about which the addict has testified, or is so at the time of testifying, Judge McDowell regarded as unsound. The rule is based on the theory that narcotic drug addicts are stupefied by such drugs, like people who are not accustomed to their use, and that their powers of observation, memory and narration are temporarily impaired. It would be contrary to all experience, however, if the usual dose of a morphine addict were to affect him exactly as that drug affects people who are not accustomed to it. There is much room for doubt if the usual dose of a morphine addict

stupefies him, or if it has any effect except to prevent withdrawal pains. The medical writers seem to be agreed that whenever a morphine addict is not under the influence of at least his usual dose he is in a state which ranges from extreme discomfort to intense pain. In other words, morphine addicts should be mentally at their best when under the influence of their customary doses, and at their worst when in need of their drugs of addiction.

Evidence of morphinism on the part of a witness, if supported by competent evidence to the effect that the memory of that particular addict has in fact been impaired or by competent opinion evidence to the effect that the addiction of the witness has been for a sufficient period, or that amounts used have been great enough probably to impair the memory of the addict, clearly may be admissible. But, Judge McDowell concluded, evidence of drug addiction standing alone should not be admitted on the ground that it may have impaired the addict's memory. The addiction may have had such an effect, and it may not. There is medical authority for the assertion that long-continued addiction or a very large consumption of a narcotic drug does usually impair the memory. But not all drug addicts have been such for a long period, and some do not use and never have used large quantities of the drug of their addiction. Many medical works make no mention of impairment of memory as a result of narcotism. Evidence of addiction would, therefore, in many cases be admissible.

Nevertheless, in *Wilson* v. *United States*, 232 U. S. 563, 34 S. Ct. 347, 58 L. Ed. 728 (1913), a defendant in a criminal case, on cross-examination, admitted that she was addicted to the use of morphine and stated that she had taken her last dose of the drug at 10 o'clock that morning. The Supreme Court held that evidence was admissible. But whether or not that decision makes admissible further questions from the cross-examiner, to show that the witness is a morphine addict, is not clear. Judge McDowell thought that that was not the necessary effect of the decision. Owing to the popular belief that drug addicts are unveracious, knowledge by the jury of the bald fact of addiction would do an illegitimate injury to the credit of the witness; illegitimate, because the basis of the ruling in the case just cited was not a probability of mendacity but a probability of some degree of still continuing temporary stupefaction of the mental powers of the witness, due to the recent dose of morphine.

In affirming the judgment of the district court in favor of the plaintiff, the Circuit Court of Appeals, Fourth Circuit, said:

> As she (the witness) had testified that her condition was due to her injuries and the evidence tended to contradict her, it was competent for that purpose. But it is insisted that it should have been received for all purposes, principally for the purpose of showing she was a dope addict, and that dope addicts are incredible. Without entering upon a discussion of the tendency, if any, of the excessive use of morphine to undermine the moral attributes of the user, it suffices to say there is no sufficient evidence in the record to show that Mrs. Huddle had made such excessive use of it, and the court committed no error in restricting the evidence.

Workmen's Compensation: Hernia or Hydrocele.—About ten months after an alleged blow on the abdomen in the course of his employment, the claimant filed his application for compensation under the workmen's compensation act, asserting that the blow had caused a hernia. An order of the workmen's compensation board awarding compensation was affirmed by the circuit court, Harlan County, and an appeal was taken to the Court of Appeals of Kentucky. The claimant testified that after the injury he was examined by about thirty physicians, all of whom advised him that he had a hernia, but he was unable to give the name of any physician but one, who himself denied ever having examined the claimant after he was injured. A physician testifying on behalf of the claimant said that the claimant was not able to do manual labor, that his ruptured condition could have been caused by such an accident as the claimant described, that the claimant had a hydrocele near the hernia, and that because the claimant was anemic and had tuberculosis, it was his opinion that the claimant was not a good surgical risk and ought not to undergo a surgical operation. On the other hand, the physician named by the claimant as having examined him testified that he had never seen him nor treated him after the injury, but that his records showed that the claimant was examined before he entered the service of his employer from whom he was now claiming compensation and that at that time he was not ruptured, but had a hydrocele and some tenderness, which would not interfere with his work. Another physician testified that he had examined the claimant after the injury, preparatory to giving evidence, by the use of the x-rays and by physical examination, that there was no evidence of hernia, that he had a hydrocele of long standing which was not due to trauma, and that while his condition might interfere slightly with his work, it could be relieved by a simple operation. The Court of Appeals, however, affirmed the order of the circuit court, Harlan County, which had affirmed the order of the workmen's compensation board, awarding compensation to the claimant because of his alleged hernia arising from an injury in the course of his employment. —*Mary Helen Coal Corporation* v. *Hooker (Ky.)*, *35 S. W. (2d) 535.*

Wills: Testimony of Attending Physician Concerning Competence of Testator.—An attending physician may express an opinion concerning the competence of a testator without giving the reason on which his opinion is based. This rule applies with greater force when the witness is the family physician, one who has known and attended the testator over a period of years and has thereby become intimately acquainted with his physical and mental constitution and peculiarities. His testimony, under such conditions, is more than a mere opinion. It is equivalent to knowledge.—*Davidove* v. *Duvall (Md.)*, *153 Atl. 417.*

Frontal Sinusitis Attributed to Trauma.—The plaintiff in falling struck her head against a wall. The impact was so severe as to cause swelling and tenderness over her left eye and resulted in pus forming in the sinus above the eye. She was operated on for the sinus trouble. The wound healed quickly, but she was suffering at the time of the trial from conjunctivitis and impaired vision. The Kansas City Court of Appeals, Missouri, held that an instruction that allowed the jury to conclude that the injury was permanent was not erroneous.—*Burnison* v. *Saunders (Mo.)*, *35 S. W. (2d) 619.*

Wills: Criteria of Testamentary Capacity.—Neither sickness nor impaired intellect is sufficient, alone, to render a will invalid. If at the time of the execution of the will the testator was capable of recollecting her property and the natural objects of her bounty and their claims on her, and knew the business about which she was engaged and how she wished to dispose of her property, that is sufficient. Moreover, those who would impeach a will on the ground that the decedent was incompetent must clearly prove that incompetence.—*Tabb* v. *Willis (Va.)*, *156 S. E. 556.*

Evidence: Medical Witness's Discussion of Facts with Others.—In a personal injury suit, the defendant, over the plaintiff's objection, asked one of the plaintiff's medical witnesses if he had conferred with other physicians in attendance on the plaintiff. Objection was made on the ground that the inquiry sought to elicit an immaterial fact. We believe, said the Supreme Court of Oregon, that the information sought was material; it is always permissible to ask a witness whether he discussed the facts with any other person.—*Stotts* v. *Wagner (Ore.)*, *295 P. 497.*

Drunkenness: As Excuse for Delay of Trial.—Intoxication resulting from the recent use of ardent spirits is no excuse for crime and the court of criminal appeals of Texas doubted whether it would be justified in establishing a precedent that one who is drunk may rely on that fact as an excuse for not going to trial on a criminal charge.—*Perry* v. *State (Texas)*, *33 S. W. (2d) 1072.*

Society Proceedings

COMING MEETINGS

Mid-South Post-Graduate Medical Association, Memphis, Tenn., February 9-12. Dr. A. F. Cooper, Bank of Commerce Building, Memphis, Secretary.

Society of American Bacteriologists, Baltimore, December 28-31. Dr. James M. Sherman, Cornell University, Ithaca, N. Y., Secretary.

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Heart Journal, St. Louis

7: 1-132 (Oct.) 1931

*Further Report on Prognosis of Angina Pectoris and Coronary Thrombosis: A Study of Five Hundred Cases of Former Condition and of Two Hundred Cases of Latter. P. D. White and E. F. Bland, Boston.—p. 1.
*Electrocardiogram in Luetic, Arteriosclerotic and Rheumatic Heart Disease. A. Friedlander, Cincinnati.—p. 15.
Nervous and Mental Influences in Angina Pectoris. S. R. Roberts, Atlanta, Ga.—p. 21.
Contributory Factors in Coronary Occlusion. D. Luten, St. Louis.—p. 36.
*Familial Tendency of Coronary Disease. J. H. Musser and J. C. Barton, New Orleans.—p. 45.
Red Cell Sedimentation Time in Coronary Occlusion. M. A. Rabinowitz, C. Shookhoff and A. H. Douglas, Brooklyn.—p. 52.
Cardiovascular Disease: Report of 398 Cases Coming to Necropsy. A. M. Glazer, Cincinnati.—p. 66.
*Ventricular Paroxysmal Tachycardia: Report of Case in Pregnant Girl of Sixteen Years with Apparently Normal Heart. T. M. McMillan and S. Bellet, Philadelphia.—p. 70.
Anomalous Papillary Muscle Attached to Pulmonary Valve of Heart. D. C. Collins, Rochester, Minn.—p. 79.
*Clinical Signs of Occluding Thrombi of Left Auricle. S. P. Schwartz and S. Biloon, New York.—p. 84.
Case of Acute Coronary Occlusion with Roentgenographic Evidence of Early Development of Aneurysm of Left Ventricle. C. Shookhoff and A. H. Douglas, Brooklyn.—p. 95.

Prognosis of Angina Pectoris.—White and Bland made a clinical study of 500 cases of angina pectoris and of 200 cases of coronary thrombosis. They present an analysis of certain factors the presence of which may or may not influence the gravity of the prognosis. The importance of the subject is evident because of the increasing frequency of angina pectoris and of the responsible position in the community of many of the patients. Of the series of 500 patients with angina pectoris, 213 are dead with an average duration of life of 4.4 years after the onset of the disease. The average duration of life to date for the total series of 500 patients was 4.9 years. Of the patients who died, death could be attributed to failure of the heart in 82 per cent, and a sudden exitus was frequently encountered. About one fifth (19 per cent) had normal hearts on physical examination, normal blood pressures, and normal electrocardiograms. This combination of observations was an unusually favorable sign. Coronary thrombosis, although frequently encountered, did not affect appreciably the duration of life, provided the patient survived the acute attack. The presence of hypertension appeared not to be of serious import. The electrocardiogram was of little help in predicting the outcome, although a "coronary" type of T wave in lead I or II was seen more often in the patients who died early. The presence of syphilis, angina decubitus, poor heart sounds, definite cardiac enlargement, congestive failure, or marked arteriosclerosis appears to be unfavorable, and the more of these factors present in the given case, the worse is the prognosis. A vital factor in the prognosis is the degree of care to which the patient can and will submit; the more careful the life of the individual, the longer as a rule will he live. Of the series of 200 patients with coronary thrombosis 101 are dead, with an average duration of life following the attack of 1.5 years. The average duration to date for the entire series of 200 patients was 2.4 years. The patients who died almost invariably succumbed to failure of the heart. The younger patients as a rule lived a little longer; the sex appeared to be unimportant. Neither the previous occurrence of angina pectoris nor its duration prior to the attack of coronary thrombosis seemed to matter. Hypertension was not important. Syphilis was rarely encountered. Cardiac enlargement of considerable degree was a somewhat unfavorable sign, while the presence of congestive failure and poor heart sounds added considerably to the gravity of the prognosis. The electrocardiogram did not help appreciably in this series. Good treatment was important.

Electrocardiogram in Heart Disease.—In a study of 100 cases of advanced cardiovascular syphilis, using like numbers of cases of arteriosclerotic and rheumatic heart disease for comparison, Friedlander did not note any electrocardiographic changes pathognomonic of syphilitic heart disease. The electrocardiographic picture in syphilitic and in arteriosclerotic disease shows a striking parallelism. The variations from the normal as found are due to the myocardial degeneration and are not characteristic of the syphilis alone. While it is true that certain of the arrhythmias and certain abnormalities of the T wave are of sinister prognostic import, it appears to be quite true that this is the case in the arteriosclerotic as well as in the syphilitic cases. There is thus no characteristic electrocardiographic picture of cardiovascular syphilis, and it is not justifiable to make definite forecasts of the prognosis in this disease from the electrocardiogram alone.

Familial Tendency of Coronary Disease.—Musser and Barton advance the thesis that there are two quite distinct expressions of coronary occlusion. The one is observed in elderly individuals, possessors of a well marked sclerosis of the arterial tree as a whole and in whom the etiologic factors are those of arteriosclerosis in general and represent largely the effects of senescence. The other occurs in men, as a rule, not past the sixth decade of life who do not have generalized arteriosclerosis, who may have relatively slight, but never exaggerated, hypertension, who have been singularly free from past infections, and who often give a history of coronary occlusion in several members of their family.

Ventricular Paroxysmal Tachycardia.—McMillan and Bellet report a case of ventricular tachycardia in which the following interesting features were noted: (1) the youth of the patient (sixteen years); (2) the absence of any definite evidence of a damaged heart; (3) the occurrence of the disturbance during pregnancy and its failure to disappear on the termination of gestation; (4) the ready abolition of the tachycardia by quinidine, and (5) the successful and uneventful outcome of a cesarean section performed during the tachycardia.

Occluding Thrombi of Left Auricle.—Schwartz and Biloon give the case histories of three patients in whom a clinical diagnosis of an occluding thrombus of the left auricle suspected during life was confirmed by postmortem examination. Two of these patients had mitral stenosis and one had hypertension. In one patient the diagnosis of a ball thrombus was suspected on the basis of the sudden and transitory appearance of peripheral vascular disturbances, such as uniform discoloration with cadaveric appearance of the extremities at a time when pulsations of the vessels to these limbs were totally absent. During such periods the sensorium was disoriented, the patient was in mild shock, the skin was cold, moist and clammy, and the first heart sound was inaudible, while oscillometric readings of the limbs affected did not reveal any movements. A diagnosis of an occluding auricular thrombus was based in one case on the rapid development of uniform discoloration with gangrene of the terminal phalanges of the ten toes and ten fingers, which persisted for more than a month until death. In the other case this diagnosis was based on the rapid progressive appearance of pain and gangrene of the legs and arms, with weak pulsations in the vessels supplying these limbs. All three patients showed auricular fibrillation with a rapid ventricular rate and were refractory to large doses of digitalis. It is probable that the irregular heart action favored the rapid development and increase in size of the auricular thrombi. The circumstances responsible for the formation of ball or pedunculated thrombi are still unknown. The mechanics of gangrene formation in the presence of an occluding thrombus of the left auricle is based on its obstruction of the mitral orifice causing a diminished blood flow to the periphery. This is enhanced by the further incomplete diastolic filling of the left ventricle because of the rapid and irregular heart action. The onset of such peripheral disturbances in patients with heart disease is of grave prognostic significance, for death takes place shortly after their appearance.

American Journal of Diseases of Children, Chicago

42: 965-1052 (Oct.) 1931—Part II

*Skin Temperatures of Children. F. B. Talbot, Velma Bates, Eleanor Bates and Alice J. Dalrymple, Boston.—p. 965.

Skin Temperatures of Children.—Studies of skin temperatures of children made by Talbot and his co-workers by means of a thermocouple showed the following facts: 1. There is a local variation of the temperature of the skin over different parts of the body, even in normal children, the temperature of the trunk being highest, the face next and the extremities lowest. The temperature of the feet tends to be lower than the temperature of the hands. 2. Surrounding temperature has a definite effect on the temperature of the skin of the body even when the child is clothed. The cooler the room is, the lower the temperature of the skin. 3. There is also a seasonal effect on the temperature of the skin. 4. This investigation showed that humidity within the limits of room temperature and room humidity studied had no effect on the temperature of the skin. 5. There is a rapid loss of heat from the surface of the body on exposure. This affects the face least, the body next and the extremities most. There is a greater variation in the reaction of the extremities to different surrounding temperatures than in other parts of the body. This suggests that the extremities act as safety valves for the conservation or the elimination of heat. 6. During fasting the temperature of the skin, as well as that of the body, becomes reduced. 7. Exercise has a definite effect on the skin temperature. During the first few minutes of exercise the temperature of the skin falls and later rises. This may be of profound physiologic importance and suggests that when exercise is first commenced heat is retained in the body in order to increase the efficiency of the muscles. 8. This work gives further evidence that the heat-regulating apparatus of the premature infant is not developed. The temperature of the skin, as well as that of the body, is affected directly by the surrounding temperature and to a greater degree than it is in normal babies. 9. Studies were made of the effect of fever on subjects with different body temperatures. These were grouped in such a way that the skin temperature for different fevers and different room temperatures are now available and are presented as possible standards of expected skin temperatures for different body and room temperatures. 10. The skin temperature was recorded in a number of cretins with lowered basal metabolism. Some of them were also studied after the metabolism had been elevated by the use of thyroid extract. When heat production was found increased, the temperature of the skin was increased. 11. A variety of pathologic cases were studied without showing any relationship between the temperature of the skin and the type of illness which the patients were suffering.

American J. Obstetrics & Gynecology, St. Louis

22: 501-660 (Oct.) 1931

*Use of Anterior Pituitary Luteinizing Substance in Treatment of Functional Uterine Bleeding. E. Novak and G. B. Hurd, Baltimore.—p. 501.

*Results of Rabbit Ovulation Test in Diagnosis of Pregnancy. K. M. Wilson and G. W. Corner, Rochester, N. Y.—p. 513.

Clinical Importance of Sex Hormones. E. C. Dodds, London, England.—p. 520.

Morphology of Menstrual Blood and Its Diagnostic Value. S. H. Geist, New York.—p. 532.

Reradiations in Radium Therapy of Carcinoma of Cervix Uteri. G. Gray Ward and Lilian K. P. Farrar, New York.—p. 543.

Five to Fifteen Year Follow-Up Study of One Hundred and Ninety-Two Cervical Cancers. F. W. Lynch, San Francisco.—p. 550.

Conclusions from Study of Five-Year Cures in Series of One Hundred and Twenty-One Cases of Carcinoma of Cervix Uteri. H. S. Crossen, St. Louis.—p. 559.

Basal Metabolic Rates in Late Pregnancy and Puerperium. O. H. Schwarz and C. Drahkin, St. Louis.—p. 571.

*Clinical Study of Postoperative Value of Barbituric Acid Hypnotics. Alice F. Maxwell, San Francisco.—p. 579.

Prevention and Repair of Hernia in Low Median-Line Incisions. J. C. Masson, Rochester, Minn.—p. 596.

*Length of Labor. L. A. Calkins, Kansas City, Mo.; J. C. Litzenberg, Minneapolis, and E. D. Plass, Iowa City.—p. 604.

Treatment of Vertex Occipitoposterior Position. A. H. Bill, Cleveland.—p. 615.

Prognosis in Nephritis Complicating Pregnancy. H. J. Stander and C. H. Perkham, Baltimore.—p. 626.

Blood Sugar in Eclampsia. J. M. Laferty, Philadelphia.—p. 637.

Is Salpingitis a Factor in Incidence of Tubal Pregnancy? R. C. van Etten, New York.—p. 645.

Case of Rudimentary Congenital Heart in the New-Born. J. I. Kushner, New York.—p. 647.

Anterior Pituitary Luteinizing Substance in Treatment of Functional Uterine Bleeding.—Novak and Hurd describe the results they obtained in the treatment of fifty-one women with functional uterine hemorrhage by an anterior pituitary luteinizing principle derived from the urine of pregnant women. In forty-four of these the treatment was successful in checking the bleeding, even though some of the patients were treated with preparations of somewhat uncertain luteinizing potency. Most of the failures were in this group. Previous efforts at the organotherapy of this condition have been unsuccessful. Radiotherapy is highly undesirable in young women, so that, because of the frequent intractability of functional hemorrhage, many patients have had to submit to repeated curettage. With strongly luteinizing preparations, it was possible to check functional hemorrhage in twenty-seven of twenty-nine cases. In fourteen of the fifty-one cases the bleeding ceased after a single injection, and in twelve after two injections. A large proportion of these were of the intractable and recurrent type, many of the patients having had from one to four or more curettages. With less potent luteinizing preparations the results were less impressive but, on the whole, satisfactory. The authors' experience with the entire group has convinced them of the value of the treatment in functional hemorrhages, and of its even greater future possibilities.

Rabbit Ovulation Test in Diagnosis of Pregnancy.—Wilson and Corner present results obtained from the urines of 196 women on whom the rabbit ovulation test as suggested by Friedman was made. The observations correspond closely to those reported in the use of the Aschheim-Zondek reaction, with apparently a small percentage of error. Its advantages over the latter are found chiefly in the much shorter time necessary, its simplicity, and a possible economy of laboratory animals. From their experience the authors believe that it should prove to be an extremely valuable and practical method for the early diagnosis of pregnancy. In their series, with the exception of a single case of endometrial hyperplasia, a positive reaction always indicated the presence of active fetal tissue in biologic contact with the maternal blood stream, or recently (not over seventy-two hours) separated from it. A negative reaction does not entirely exclude the possibility of a pregnancy being present, since the intra-uterine or extra-uterine ovum may have perished and been retained for some period of time. The test may prove to be of some value in determining the life or death of the ovum in the early months, though not its immediate death, and not in the later months of pregnancy.

Study of Postoperative Value of Barbituric Acid Hypnotics.—Maxwell calls attention to the fact that opium and its derivatives increase the frequency and severity of postoperative distention and vomiting and are not necessary to relieve pain. Barbituric acid hyptonics are satisfactory from a pharmacologic and clinical standpoint when combined with an analgesic (amidopyrine). It is illogical to combine these agents in fixed proportion, because of the marked difference in their rate of elimination; it is rational to administer them separately according to clinical indications. Barbital, by virtue of its simple chemical structure, is less toxic and clinically as effective as its more complex and toxic modifications. The author recommends these hypnotics because their action is limited to the central nervous system and their use is followed by a high incidence of amnesia and by little disturbance of organic function.

Length of Labor.—Calkins and his associates believe that a more accurate observation of the resistance of the cervix (and the pelvic floor), as well as more accurate determination of the effectiveness of the labor pains, will be necessary in order to analyze the causes for the extreme variations in the length of labor so commonly encountered. More accurate determination of the resistance would likewise enable one to predetermine the probable duration of the labor. Deliberate appraisal of the various factors present in any given labor, when balanced against a more definite knowledge of the forces present and functioning, might also serve to reduce the present high rate of operative intervention. To this end, it is sug-

gested that the consistency of the cervix, as well as the thickness of its wall and the length of its canal, be accurately determined and recorded before labor begins or as early in labor as possible. Such a record on a scale of five (one being a very soft cervix, three one of average softness, and five a firm resistant cervix) has been kept in a few hundred cases with surprisingly satisfactory results. It is suggested that the effectiveness of labor pains be more accurately determined and recorded for the purpose of increasing one's ability to determine the probable length of labor in each given case. Experience with a small series thus estimated on a scale of five (with one and two representing poor pains, three average pains, four hard pains, and five abnormally hard pains), has proved highly suggestive. In the grading of labor pains, more attention is paid to the intensity of the contraction than to duration or frequency, although all three factors must be given consideration. Intensity of first stage contractions can be satisfactorily estimated by digital (not palmar) palpation of the fundus or by palpation of the tension, and amount of stretching, produced in the cervix. Likewise, in the second stage, digital palpation of the fundus is preferred to the determination of the amount of descent or the amount of stretching of the pelvic floor. It is believed that accurate determination of the effectiveness of the labor pain balanced against the resistance of the cervix and pelvic floor is the all important factor in determining the length of labor. The other variants, as analyzed by the authors, are of only minor importance.

American Journal of Public Health, New York

11: 1189-1300 (Nov.) 1931

Presidental Address. H. S. Cumming, Washington, D. C.—p. 1189.
Drought and Health. M. P. Ravenel, Columbia, Mo.—p. 1196.
1930-1931 Drought and Its Effect upon Public Water Supply. E. S. Tisdale, Charleston, W. Va.—p. 1203.
Sewage Disposal Difficulties Due to Drought. L. S. Finch, Indianapolis. —p. 1219.
Epidemiologic Study of Suspected Water-Borne Gastro-Enteritis. M. V. Veldee, Washington, D. C.—p. 1227.
What a Public Health Nurse Expects of Her Chief—the Health Officer. Agnes J. Martin, Syracuse, N. Y.—p. 1236.

Annals of Internal Medicine, Ann Arbor, Mich.

5: 401-538 (Oct.) 1931

*Variations in Manifestations of Rheumatic Fever in Relation to Climate. W. T. Longcope, Baltimore.—p. 401.
*Colonic Changes in Chronic Arthritis. W. H. Dickson, Toronto. —p. 408.
*Total Occlusion of Right Branch of Pulmonary Artery by Organized Thrombus. J. H. Means and T. B. Mallory, Boston.—p. 417.
*Therapeutic Use of Oxygen in Heart Disease. A. L. Barach, New York.—p. 428.
*Reaction to Nitrites in Anginal Syndrome and Arterial Hypertension. A. M. Burgess, Providence, R. I.—p. 441.
*Auricular Flutter and Complete Heart Block: With Restoration of Sinus Rhythm and A-V Conduction. L. T. Gager, Washington, D. C. —p. 463.
Primary Aplastic Anemia: Two Cases. J. B. Carey and J. H. Taylor, Minneapolis.—p. 471.
*Use of Sulphur for Production of Fever in Peripheral Vascular Diseases. L. M. Waller and E. V. Allen, Rochester, Minn.—p. 478.
*Mediastinal Displacement in Pneumothorax. W. C. Pollock, Denver. —p. 486.
Treatment of Recurrent Erysipelas. H. L. Amoss, Durham, N. C. —p. 500.
Historical Development of Present Conception of Cardiac Conditions in Exophthalmic Goiter. A. M. Ginsberg, Kansas City, Mo.—p. 505.

Manifestations of Rheumatic Fever in Relation to Climate.—According to Longcope, the available statistics concerning the geographic distribution of rheumatic fever indicate that the disease is rare or almost unknown in the tropics, and much less commonly observed in the warmer portions of mid-temperate zones than in the colder portions. In some regions where rheumatic arthritis is said to be rare, mitral stenosis is quite frequently observed. At the Johns Hopkins Hospital in Baltimore the admission rate to the adult medical wards for rheumatic fever, in all its forms and in all its stages, over a period of five years was 1.37 per cent. The necropsy rate for rheumatic heart disease over a period of twenty-one years was 1.66 per cent. The disease, therefore, is comparatively common. An analysis of 142 cases of rheumatic fever studied during this period showed that symptoms or signs of cardiac disease appeared in the past histories of 50 per cent of the cases. Cardiac disease was present on admission to the hospital or was detected during observation in 95 per cent of these cases. Only 6 of the entire 142 patients presented symptoms and signs of arthritis alone, but in more than 77 per cent arthritis, often of mild degree, occurred at some time during the illness for which they were admitted to the hospital. Rheumatic fever, as it is seen at the Johns Hopkins Hospital, is essentially a disease of the heart, frequently preceded or accompanied by arthritis, often of mild degree, or by chorea. Severe acute arthritis is rarely seen, but acute pericarditis and pleurisy are not very infrequent. The author suggests that the infrequency of severe acute arthritis, the great frequency of carditis and the comparative insidiousness of the disease during the acute and subacute stages render the clinical picture of rheumatic fever somewhat different in Baltimore from that generally described for more northerly sections of the United States.

Colonic Changes in Chronic Arthritis.—Dickson gave barium enemas to normal rats, well nourished and fed on a diet rich in vitamin B. After this examination a diet deficient in vitamin B was exhibited for several weeks, when a second enema was given. The diet was again returned to one high in vitamin B and a third enema administered in a month's time. The colon underwent marked changes during the observation. The second examination showed the bowel elongated and markedly atonic, so atonic in fact that the pressure from the flow of the enema was great enough to rupture the colon, and the enema poured out into the abdominal cavity. The rats not lost by this accident were at once placed on a diet again rich in vitamin B, and further observation was made in a month's time. At the third observation the tone of the intestine had returned to normal, and the intestine was much shortened in its total length. In some of the rats it was difficult to demonstrate any difference between appearances at the first and at the third enema. With this point in mind, the author assumed that some of the abdominal disturbances of chronic arthritis might be associated with nutritional deficiency, and investigation was undertaken in an attempt to prove or disprove the theory. The first step was to demonstrate the incidence and type of colonic abnormalities in arthritic cases. When this had been done, periodic examinations were made to demonstrate the effect of suitable diet on the clinical progress and the roentgenologic appearance of the large intestine. In many cases the return to a normal appearance was indeed amazing. In others, and these were complex cases in which nutrition alone played only a minimum part, the changes were slight or absent. It was, however, extremely interesting to note that in the majority of cases the improvement noted on the film bore a close relation to the improvement noted clinically. Latterly, the author has been able with a fair degree of accuracy to state from the roentgenologic examination the amount of improvement, shown clinically, without any progress history being supplied from the clinician. Also it has been possible after the first examination in some cases to give a prognosis pointing toward failure that has been borne out by the patient's subsequent course.

Occlusion of Right Branch of Pulmonary Artery by Thrombus.—Means and Mallory report a case which illustrates the fact that total thrombotic occlusion of a main branch of the pulmonary artery may occur without damage to the lung, provided it develops slowly enough to allow for the development of collateral circulation through the bronchial system. Such a lesion may not produce local signs in the lungs, but the presence of cyanosis and right-sided heart failure without other obvious cause may suggest its presence. The case is interesting from the point of view of morbid physiology in that it proves that an entire lung may be separated from its pulmonary artery supply and suffer no injury of any sort provided the occlusion is gradual, allowing time for the establishment of collateral circulation from the aorta. The situation reminds one of those cases of chronic total occlusion of both coronaries without history of the characteristic picture of coronary occlusion. The effect of slow closure of the pulmonary artery is evidently different from sudden shutting off, as from embolism or ligation, in which cases the picture of infarction is produced.

Use of Oxygen in Heart Disease.—Barach studied the therapeutic use of oxygen in eight patients with congestive heart failure due to primary cardiac disease, in five cases of

cardiac insufficiency developing as a sequela to chronic pulmonary diseases, in four cases of acute coronary thrombosis, and in three cases of coronary arteriosclerosis with chronic cardiac pain. In the cases of congestive heart failure the most striking effects observed were relief of dyspnea and orthopnea, diuresis and disappearance of edema, and a marked rise in the carbon dioxide content of the arterial blood. Other observations noted were relief of cyanosis, increased arterial oxygen saturation, decreased pulmonary ventilation, lowered pulse rate, and decrease in the lactic acid content of the blood. In cases of acute coronary thrombosis, life appeared to be prolonged by the inhalation of an oxygen-enriched atmosphere until the heart was able to recover from its acute functional disturbance. The cases of coronary arteriosclerosis with chronic cardiac pain were relieved by residence in a high oxygen atmosphere. These results indicate that oxygen want is the primary factor in the production of many forms of cardiac dyspnea. The increase in carbon dioxide content of the arterial blood occurs as an adaptative change which facilitates the elimination of carbon dioxide. The clinical improvement which patients suffering from the various forms of heart failure experience suggests a new employment of oxygen therapy by effective methods in these conditions.

Reaction to Nitrites in Arterial Hypertension.—Burgess states that, except for a transient fall in blood pressure after amyl nitrite, neither it nor glyceryl trinitrate when used in the usual therapeutic doses causes any consistent blood pressure changes in normal human beings or in persons with arterial hypertension with or without severe renal damage or retinal arteriolar sclerosis. The fall occurring after the use of amyl nitrite is so rapid and transitory and so independent of subjective symptoms that it is impossible to measure it accurately by taking blood pressure determinations in the ordinary way. This fact greatly decreases its usefulness as a test for arteriolar relaxability in estimating the prognosis in arterial hypertension. In persons suffering from attacks of angina pectoris of the usual ambulatory type, a rapid fall in systolic and usually in diastolic pressure takes place after the use of these drugs. The pain relief that occurs in these cases of ambulatory angina is independent of the pressure levels, and therefore apparently independent of the action of the nitrites on the peripheral vessels, but due to their action in increasing coronary circulation. The cause of the pain in ambulatory angina is probably an ischemia of the myocardium dependent on an insufficient blood supply due to disease of the coronary arteries.

Auricular Flutter and Complete Heart Block: With Restoration of Sinus Rhythm and Auriculoventricular Conduction.—Gager restored a patient with complete heart block to sinus rhythm and auriculoventricular conduction by the use of quinidine sulphate. Physical and mental improvement resulted. Fifteen cases were found in the literature showing the association of auricular flutter and total block, and the clinical phenomena and criteria for diagnosis are reviewed. From experimental and clinical observations in partial block and from the results in three cases of complete block, the author shows the value of restoring sinus control in cases of auricular flutter.

Sulphur for Production of Fever in Peripheral Vascular Diseases.—Waller and Allen made observations on pain at the site of injection, on relief of pain in ulcerated or gangrenous regions, on healing of ulcers, on height and duration of fever, and on chill and leukocytosis in fifteen cases of peripheral vascular disease, in which thirty-two intramuscular injections of sulphur, 2 per cent, in olive oil were given. Fever began about seven hours after the injection; the temperature reached an average maximal level of 102 F. and lasted an average of fifty hours. Chills occurred following approximately 50 per cent of the injections, but they were mild when doses of suspension of sulphur of 1.5 or 2 cc. were given. The most satisfactory dose in the treatment of peripheral vascular disease was 1.5 or 2 cc. Greater amounts were rarely necessary to produce effect even later in the course of the injections. Clinical improvement was as marked following intramuscular injection of sulphur as that induced by intravenous injection of typhoid vaccine, and occasionally it was more striking. The pain at the site of the injection varied from moderate to severe and constituted the greatest disadvantage to intramuscular injection of sulphur in olive oil. Sulphur in olive oil, injected intramuscularly, in the treatment of peripheral vascular disease, is most satisfactory for persons of advanced age, for those who are resistant to treatment by vaccine, and for those in whom the pain from the injection is not excessive.

Mediastinal Displacement in Pneumothorax.—Pollock gives roentgen evidence that a disturbance of the normal physiologic intrathoracic pressure during the course of artificial pneumothorax therapy may produce mediastinal displacement when the mediastinum is sufficiently flexible. Mediastinal displacements eventrating into the contralateral lung during the phase of expiration are not of clinical significance. However, fixed displacements in the presence of a relatively nonelastic mediastinal pleura produced by excessive pressure in the pneumothorax cavity may give rise to respiratory embarrassment and a sense of pressure to the stage of discomfort. A reduction of the displacement results in comfort to the patient. Mediastinal displacement depends on flexibility of the mediastinum, the intrathoracic pressure in the pneumothorax cavity, and the relative fixation of the mediastinal contents. A relatively flexible mediastinum usually occurs in younger adults early in artificial pneumothorax treatment, and the mediastinum tends to become less and less flexible as pneumothorax therapy is continued.

Archives of Dermatology & Syphilology, Chicago

24: 537-724 (Oct.) 1931

Sensitizations: Regional, Seasonal, Dietary and Other Influences Accounting for Variations and Fluctuations. M. B. Sulzberger, New York, and R. L. Mayer, Breslau, Germany.—p. 537.
Allergic Skin Reaction. H. L. Alexander, St. Louis.—p. 543.
*Bacterial Protein Fever in Treatment of Syphilis in Rabbit. J. A. Kolmer, Philadelphia.—p. 546.
Eczema Due to Fungi: Report of Case in an Eighteen Months Old Baby. S. M. Peck and G. Salomon, New York.—p. 554.
Schizosaccharomycosis: I. Present Status of Identification of Schizosaccharomyces Hominis and Its Results. T. Benedek, Leipzig, Germany.—p. 557.
*Proliferative Gingivitis of Pregnancy: Cases. S. Monash, New York.—p. 580.
Leukemia Cutis: Case. F. R. Schmidt, Chicago.—p. 587.
*Syphilitic Bursopathy of Verneuil. V. C. Garner and A. G. Schoch, Philadelphia.—p. 591.
*Dermatitis Venenata Due to Shoe Leather: Two Cases. G. M. Lewis, New York.—p. 597.
Xanthoma Diabeticorum: Case. H. J. Templeton and E. E. Chouret, Oakland, Calif.—p. 604.
Kerion Microsporicum with Hematogenous and Ectogenous Microsporids: Case, with Reference to Literature. A. Blumenfeld, Boston.—p. 607.
Macular Atrophy of Skin. L. Chargin and H. Silver, New York.—p. 614.

Protein Fever in Rabbit Syphilis.—Kolmer found that the intravenous injection of typhoid-paratyphoid vaccine into syphilitic rabbits in doses of from 1,000,000 to 100,000,000 per kilogram of weight produced a rise of rectal temperature of from 2 to 4 or 5 degrees Fahrenheit, lasting several hours and reaching the preinjection level within twenty-four hours. The treatment of rabbits with acute testicular syphilis with ten intravenous injections of increasing amounts of typhoid-paratyphoid vaccine at intervals of seventy-two hours did not result in complete cure in any of the animals. Ten intravenous injections of the vaccine at intervals of seventy-two hours, together with five intravenous injections of arsphenamine in doses of 0.002 Gm. per kilogram at weekly intervals, did not result in the complete cure of any of the rabbits with acute testicular syphilis. Ten intravenous injections of the vaccine at intervals of seventy-two hours, together with five intramuscular injections of potassium bismuth tartrate in doses of 0.001 Gm. per kilogram at weekly intervals, did not result in the complete cure of any of the rabbits. The intravenous injection of from 0.008 to 0.4 cc. of Coley's fluid per kilogram of weight into syphilitic rabbits produced a rise of rectal temperature of from 3 to 5 or 6 degrees Fahrenheit which lasted several hours and which reached the preinjection level within twenty-four hours. None of the rabbits with acute testicular syphilis that received ten intravenous injections of increasing amounts of Coley's fluid at intervals of seventy-two hours were completely cured. The rabbits with acute testicular syphilis that received ten intravenous injections of arsphenamine in doses of 0.002 Gm. per kilogram or five intramuscular injections of potassium bismuth

tartrate in doses of 0.001 Gm. per kilogram at weekly intervals were not completely cured. In the rabbits given intravenous injections every two days of 1 cc. of citrated blood taken from human beings from twenty-four to thirty-six hours after malarial paroxysms there was no rise in temperature, and demonstrable effects on the course of the acute testicular syphilis were not noted. Therefore, the fever of from 2 to 5 degrees Fahrenheit, which lasted several hours and which was induced in rabbits by intravenous injections of increasing amounts of typhoid-paratyphoid vaccine and Coley's fluid, showed much less effect on the course of acute testicular syphilis than the fever induced by hot baths. While the treatment for acute and chronic syphilis in human beings with intravenous injections of typhoid-paratyphoid vaccine and Coley's fluid alone or in combination with chemotherapy has yielded encouraging results, these agents have been without pronounced curative activity in the treatment for acute testicular syphilis in rabbits.

Gingivitis of Pregnancy.—Monash reports several cases in which growths were observed on the gums of pregnant women. They began to form at a variable time during pregnancy, usually during the earlier months, increased in size unless treated, and spontaneously diminished or disappeared after delivery of the child. The growth is usually part of a generalized gingivitis and represents simply an exaggerated degree of the condition. The name "proliferative gingivitis of pregnancy" is proposed. The growth is inflammatory in origin and should not be classed as a true tumor. Prophylactic measures and treatment are discussed.

Syphilitic Bursopathy.—Garner and Schoch report two additional cases of the syphilitic bursopathy of Verneuil, bringing the present number of cases in the literature to thirty-eight. The prepatellar bursae were involved in each case, both patients being women with late syphilis. The chief clinical features of the conditions are discussed, with especial emphasis on the indolence and frequent symmetry of the process, the negative roentgenographic study, the positive Wassermann reaction and the early response to conservative antisyphilitic therapy. In one of the patients the type of scar deserves emphasis. Unlike the usual thin, atrophic scar of a cutaneous ulcerating gumma, it was depressed, dimpled and adherent to the underlying tissue, and did not give a suggestion of the configuration of the original gummatous ulcer.

Dermatitis Venenata from Shoe Leather.—Lewis reports two cases of dermatitis venenata from shoe leather, which point to the fallacy of considering all dermatoses of the feet to be of fungus origin. The condition may have escaped recognition or it is extremely rare, as it is not mentioned in any of the standard textbooks on dermatology or monographs on dermatitis venenata. A review of the literature failed to yield any reports of cases. However, it seems logical to keep the possibility of such a condition in mind when one is dealing with dermatoses of the feet, especially those that have proved refractory to ordinary methods of therapy.

Archives of Internal Medicine, Chicago

48: 537-720 (Oct.) 1931

*Treatment for Secondary Anemia: Study of Results in 126 Cases. C. S. Keefer, Boston, and C. Yang, Peiping, China.—p. 537.
Metabolism in Myotonia Atrophica: Report of Case. S. Morgulis, A. Young, J. K. Miller and E. Janecek, Omaha.—p. 569.
*Tuberculous Meningitis with Syphilitic Meningitis Terminating in Recovery: Review of Literature. D. W. Kramer and B. B. Stein, Philadelphia.—p. 576.
*Cause of Exophthalmic Goiter: Biochemical Hypothesis. W. S. Reveno, Detroit.—p. 592.
*Elimination of Phenolsulphonphthalein by Kidney: Influence of Pathologic Changes in Liver. J. P. Hanner and G. H. Whipple, Rochester, N. Y. —p. 598.
Tumors of Suprarenal Gland with Especial Reference to Carcinoma of Cortex: Case. J. Meyer and G. Frumess, Chicago.—p. 611.
*Tumors of Heart and Pericardium: Pathology, Symptomatology and Report of Nine Cases. W. M. Yater, Washington, D. C.—p. 627.
*Functional Aspects of Regenerated Hepatic Tissue. T. L. Althausen, San Francisco.—p. 667.
Normal Asymmetry and Unilateral Hypertrophy. G. Halperin, Chicago. —p. 676.
Isolated Congenital Dextrocardia: Report of Two Cases with Unusual Electrocardiographic Findings: Anatomic, Clinical, Roentgenologic and Electrocardiographic Studies of Cases Reported in Literature. S. S. Lichtman, New York.—p. 683.

Secondary Anemia.—In a study of the treatment in 126 cases of anemia due to various causes, Keefer and Yang noted the following facts: The recovery from anemia due to chronic loss of blood may be accelerated following the administration of liver and iron. In some cases, transfusion of blood was necessary owing to the severity of the anemia. Continued loss of blood in small amounts and sepsis retard recovery. Anemias resulting from inadequate or faulty diets were often associated with the avitaminoses or other deficiency disorders. Many of these patients recovered following a well balanced diet, and in some regeneration of the hemoglobin was accelerated by the use of liver or iron. The anemia associated with chronic dysentery usually appeared in patients who had been on inadequate diets and who had had active dysentery for two months or longer. Hemorrhage, infection and gastric anacidity played a minor part in the production of the anemia. In the group as a whole, all the clinical features that are said to be characteristic of pernicious anemia were observed, including atrophy of the lingual papillae, subacute combined sclerosis, gastric anacidity and anemia responding to liver extract. These observations lend support to the hypothesis that pernicious anemia is a deficiency disease. Anemia associated with infestation due to hookworm may be cured with iron, or liver and iron, while the patients continue to carry the worms. Malnutrition and faulty diets are important factors in predisposing such patients to anemia. Women with the anemias of pregnancy recover following the transfusion of blood or following the administration of liver and iron. In some cases, iron alone is positive; in others, liver or liver extract is potent in increasing the rate of recovery. Recovery from the anemia associated with kala-azar may be extremely slow in spite of treatment with antimony compounds, transfusions of blood and ingestion of liver and iron. In this condition it appears as if the damage to the bone marrow were responsible for the anemia. When recovery occurred in many of the foregoing types of anemia, the reticulocytes were increased. Generally speaking, the number of reticulocytes depends on the level of the red cell count at the beginning of the treatment, although there were exceptions in cases in which one observed relatively large increases in reticulocytes with a high red blood cell count. In most of these cases the hemoglobin content was low. In other cases an increase in the reticulocytes was not observed following treatment. In some of these cases the reticulocytes had been increased before treatment was begun; in others, they were never increased. When liver ash was given in amounts equivalent to 300 Gm. of whole liver a day, containing 21 mg. of iron, striking results were not observed. In several instances there was a moderate increase in the hemoglobin, red blood cells and reticulocytes, and this response was usually observed in patients who subsequently recovered promptly on larger doses of iron. In some cases of anemia, liver and iron were more effective than when either one was given alone. In others, the maximum effect was observed following the use of iron. Liver extract was of demonstrable value in some of the nutritional anemias of childhood, in some of the anemias associated with pregnancy and in chronic dysentery. It was of little value in posthemorrhagic anemia. From the authors' observations, it was not possible to predict in every case which form of treatment would be most beneficial. If complete recovery is not observed in patients following the use of iron, liver should be added. In many patients who do not respond to liver or iron there is usually an adequate cause to explain their failure. Infection and pathologic processes of the bone marrow are of the greatest importance. The response in various clinical anemias following the ingestion of food substances other than liver, kidney or iron needs further investigation.

Tuberculous Meningitis.—Kramer and Stein give the case history of a Negro who had evidence of syphilitic meningitis; subsequent observations of tuberculous meningitis were made, and a favorable termination is reported. A review of the literature revealed a number of contributions on the curability of tuberculous meningitis and numerous reports of cures. This number was considerably reduced because of insufficient scientific data. Seventy-three cases of presumably authentic cures were collected. A study of this group of cases does not enlighten one with information that may be of value in the

direct treatment for this disease in the future. Cures have been attributed to various factors, such as the age and the resistance of the patient and a low virulence of the organism. Statistics of the collected cases show the highest percentage of cures among patients above 20 years of age (33 per cent), and the lowest percentage in infants. The authors believe that the traditional and fixed idea that a patient with tuberculous meningitis must die should be reconsidered. No doubt, a recovery is extremely rare, but no one can foretell when this unexpected favorable termination may occur. The tendency to discard the diagnosis of tuberculous meningitis and disregard such laboratory observations as the presence of tubercle bacilli and successful inoculation into guinea-pigs, merely because the patient recovered, seems unscientific and illogical.

Exophthalmic Goiter.—Reveno advances the hypothesis that exophthalmic goiter is primarily a disturbance resulting from a long continued toxic process in the intestinal tract. This process not only damages the thyroid to the end that varying amounts of its functioning tissue are destroyed but causes a faulty and irregular metabolism of the amino-acid tyrosine, so that an excess of thyroxine, epinephrine and tyramine is produced. These conclusions are reached in view of (1) the inadequacy of the thyrogenic theory of the disease; (2) the work of McCarrison on the effects of toxic material in the intestinal tract on the thyroid; (3) the close relationship between the chemical constitution of thyroxine, epinephrine and tyramine; (4) the common source of these three substances, viz., tyrosine; (5) the changes in the normal tyrosine-tyrosinase reaction and the decarboxylization process for conversion of tyrosine to phenols, with resulting overproduction of the base tyramine, and (6) the pharmacologic action of tyramine.

Phenolsulphonphthalein Test.—Hanner and Whipple describe experiments from which it is clear that in dogs with necrosis of the liver due to chloroform poisoning there is a distinct rise in the elimination of phenolsulphonphthalein by the normal kidney. A rise in the elimination of phenolsulphonphthalein from a control level of from 75 to 78 per cent to from 90 to 97 per cent may be noted. With repair of the hepatic injury, the elimination of phenolsulphonphthalein returns to normal. Phosphorus poisoning gives a similar but less striking reaction. With experimental biliary obstruction in the dog, the same general reaction is noted, with a definite increase in the elimination of phenolsulphonphthalein by the normal kidney. After hepatic injury due to chloroform, the dog's liver does not remove phenolsulphonphthalein from the blood stream and does not excrete it in the bile, whereas in a normal dog the liver removes much phenolsulphonphthalein from the blood, and about 10 per cent of the injected phenolsulphonphthalein may be recovered from the bile within two hours. A chronic biliary fistula and an Eck fistula may permit a smaller excretion of phenolsulphonphthalein in the bile and a corresponding rise in the elimination of the dye in the urine. There is no evidence that a cholagogue, whether in the normal dog or in one with a biliary fistula, increases the elimination of phenolsulphonphthalein by way of the bile, and consequently the urinary excretion of phenolsulphonphthalein is unchanged. Phenolsulphonphthalein given by mouth is absorbed and reappears in the urine only in quantities equal to from 3 to 5 per cent of the amount administered. Reabsorption, therefore, is a negligible factor when applied to the phenolsulphonphthalein eliminated through the bile into the duodenum. From these experiments and the observations of other workers, it may be concluded that the elimination of phenolsulphonphthalein by the liver and kidney under these conditions is identical in the dog and man. Clinically, an unusually high renal elimination of phenolsulphonphthalein should suggest pathologic changes in the liver. Combined renal and hepatic disease calls for cautious analysis of the renal elimination of phenolsulphonphthalein.

Tumors of Heart and Pericardium.—According to Yater, the symptomatology of tumors of the heart and pericardium may be divided into two classes—that which is not suggestive of tumor of the heart and that which is. In the first class are those cases in which there are no symptoms referable to cardiac dysfunction, those in which there is terminal cardiac breakdown, those in which symptoms of simple congestive heart failure dominate the clinical picture, those in which sudden death occurs with or without previous cardiac symptoms, and those in which the clinical picture is that of subacute bacterial endocarditis. In the second class the clinical types may be quite diverse but should serve to call to mind the possibility of tumor of the heart. Any case of heart block in which no satisfactory explanation of the arrhythmia is obtainable may be one of tumor breaking through or originating in the main portion of the conduction apparatus. When symptoms referable to disturbance of function of a portion of the heart occur, tumor of that part of the heart is a diagnostic possibility. In the case of pedunculated intracavitary tumor obstructing a cardiac orifice, usually the mitral or tricuspid, certain deviations from the usual symptomatology of endocarditis are often present. The history of rheumatic infection is absent; the course of congestive failure is progressive; there is little or no response to digitalis, and the physical signs may change remarkably with change of posture. In every case in which tricuspid stenosis seems to be present, tumor should be suspected because inflammatory stenosis of that orifice is exceedingly rare. Acquired pulmonic stenosis should be considered the result of neoplastic obstruction. If in a person who is known to harbor a malignant neoplasm cardiac symptoms develop which cannot be otherwise explained, it is reasonable to assume that metastatic invasion of the heart has occurred. Accumulations of hemorrhagic fluid in the pericardium are suggestive of subepicardial or pericardial neoplasm, and hemorrhagic pleural effusions are not uncommon in malignant disease of the heart or pericardium. A localized enlargement of the heart or an irregularity of outline associated with enlargement as shown in the roentgenogram is suggestive of tumor of the heart as well as aneurysm and mediastinal tumor.

Regenerated Hepatic Tissue.—Althausen states that, in toxic cirrhosis of the liver, vigorous regeneration of tissue maintains the carbohydrate metabolism-regulating function and probably other metabolic activities of this organ. Owing to a loss of the original structure of the liver in this disease, the new hyperplastic nodules lack connection with bile channels, accounting in this manner for marked impairment in the excretion of dye. This information can be utilized by the clinician for differential diagnosis of toxic cirrhosis of the liver by the use of two suitable tests of hepatic function.

Archives of Pathology, Chicago

12: 521-688 (Oct.) 1931

Periarteritis Nodosa Complicated by Fatal Intrapericardial Hemorrhage: Case. B. M. Vance and J. E. Graham, New York.—p. 521.
Effects of Ultraviolet Rays, Radium and X-Rays on Proteins. Mona Spiegel-Adolf, Vienna, Austria, and Philadelphia.—p. 533.
Pseudohermaphroditismus Masculinus Externus Associated with Suprarenal Hyperplasia and Vascular Hypertension: Case. Claire E. Healey and C. C. Guy, Chicago.—p. 543.
Malignant Hemangioma of Lung with Multiple Visceral Foci: Case. Martha Wollstein, New York.—p. 562.
Experimental Scarlatinal Nephritis in Dog. C. W. Duval, New Orleans. —p. 572.
Anomalous Origin and Course of Left Coronary Artery. A. R. Kintner, Rochester, Minn.—p. 586.
Homeotransplantation and Heterotransplantation in Guinea-Pig: Effects of Graded Degrees of Heat on Cartilage and on Thyroid Gland. W. J. Siebert, St. Louis.—p. 590.

Association American M. Colleges Journal, Chicago

6: 339-400 (Nov.) 1931

Place of Postgraduate Medical Education. W. C. Rappleye, New York. —p. 339.
Premedical Education. W. D. Reid, Boston.—p. 345.
Report of Data Pertinent to Problem of Selection of Medical Students. Doris F. Twitchell, Ann Arbor, Mich.—p. 357.
Manikin Practice in Midwifery Teaching. C. B. Reed, Evanston, Ill. —p. 362.
Pioneer Medical Education in Asia. S. H. Liljestrand, Chengtu, China. —p. 366.

Journal of Clinical Investigation, Baltimore

10: 689-984 (Oct. 20) 1931

Relationship Between Environment and Basal Insensible Loss of Weight. F. H. Wiley and L. H. Newburgh, Ann Arbor, Mich.—p. 689.
Method for Determination of Heat Production Over Long Periods of Time. L. H. Newburgh, F. H. Wiley and F. H. Lashmet, Ann Arbor, Mich.—p. 703.
Improved Method for Determination of Water Balance. F. H. Wiley and L. H. Newburgh, Ann Arbor, Mich.—p. 723.

Doubtful Nature of "Luxusconsumption." F. H. Wiley and L. H. Newburgh, Ann Arbor, Mich.—p. 733.
Determination of Potassium in Cardiac Muscle and Presumable Influence of Beta Radiations on Rhythm. L. C. Scott, New Orleans.—p. 745.
*Gastric Secretion After Histamine: Its Evaluation as Quantitative Test in Digestive Disorders. G. D. Gammon and T. G. Miller, Philadelphia. —p. 755.
Mineral Exchanges of Man: III. Mineral Metabolism During Treatment of Case of Polycythemia Vera. S. H. Bassett, T. Killip and W. S. McCann, Rochester, N. Y.—p. 771.
*Insulin Absorption by Conjunctival Membranes in Rabbits. C. D. Christie and R. F. Hanzal, Cleveland.—p. 787.
*Electrocardiographic Studies During Attacks of Angina Pectoris and Other Paroxysmal Pain. M. L. Siegel and H. Feil, Cleveland.—p. 795.
Studies in Congestive Heart Failure: XIII. Relation of Dyspnea of Exertion to Oxygen Saturation and Acid-Base Condition of Blood. G. E. Cullen, T. R. Harrison, J. A. Calhoun, W. E. Wilkins and M. M. Tims, Nashville, Tenn.—p. 807.
Id. XIV. Orthopnea: Its Relation to Ventilation, Vital Capacity, Oxygen Saturation and Acid-Base Condition of Arterial and Jugular Blood. J. A. Calhoun, G. E. Cullen, T. R. Harrison, W. L. Wilkins and M. M. Tims, Nashville, Tenn.—p. 833.
Comparison of Racemization Curves for Urinary, Edema Fluid, and Blood Plasma Proteins. J. W. Cavett and R. B. Gibson, Iowa City. —p. 857.
*Nutritional Edema: Observations on Relation of Serum Proteins to Occurrence of Edema and Effect of Certain Inorganic Salts. A. A. Weech and S. M. Ling, Peiping, China.—p. 869.
Studies on Electrical Systole (Q-T Interval) of Heart: II. Its Duration in Cardiac Failure. S. N. Cheer and F. R. Dieuaide, Peiping, China.—p. 889.
*Effects of Sustained Pituitary Antidiuresis and Forced Water Drinking in Epileptic Children: Diagnostic and Etiologic Study. I. McQuarrie and D. B. Peeler, Rochester, N. Y.—p. 915.
Plasma Proteins in Relation to Blood Hydration: VI. Serum Proteins in Nephritic Edema. J. P. Peters, F. S. Bruckman, Anna J. Eisenman, Pauline N. Hald and A. M. Wakeman, New Haven, Conn.—p. 941.

Gastric Secretion After Histamine.—Gammon and Miller noted that the maximal free gastric acidity after histamine and after Liebig's extract in a miscellaneous group of patients varied to a far greater extent from the mean value than it did after the gruel meal in a similar group. No correlation could be recognized between the maximal free acidity after histamine and after a gruel meal when the two tests were done on the same group of patients. The variations in the acidity after histamine could not be correlated, except in the achlorhydrias, with the diagnoses of the cases. No significant variations in acidity or volume secretion after histamine were noted in correspondence with the age or the sex of the patients. The volume of secretion after histamine was greatest on the average in the group of cases of duodenal ulcer and duodenitis, but it bore no direct relationship to the degree of acidity, except that it was lower in those cases with zero acidity. On the basis of their observations the authors conclude that the histamine test, though valuable to determine the ability of the stomach to secrete acid, is not serviceable as a routine method of gastric analysis, because the variations in its results are great without obvious cause. The gruel meal has an advantage as a routine test of gastric acidity in that its results may be more nearly correlated with the clinical diagnoses. The explanation for the superiority of the gruel meal probably lies in the fact that it contains buffer substances which permit the stomach to adjust the acidity of its total contents to a more definite level, a level that is correlated with existing conditions.

Insulin Absorption by Conjunctiva.—Christie and Hanzal describe experiments in which they found that insulin instilled into the conjunctiva is absorbed with great rapidity and gives rise to a fairly constant and consistent fall of blood sugar levels in rabbits. The drop in blood sugar level persists for from four to five hours as against from five to six hours by the subcutaneous route. Apparently it requires about 60 per cent more insulin by this method of administration than by the subcutaneous route. The authors have seen nothing to make them believe that commercial insulin is irritating to the eyes of animals.

Angina Pectoris.—Siegel and Feil report electrocardiographic observations in eleven cases made during transient attacks of angina pectoris. In eight of these patients there was inversion of the T wave and (or) inversion of the S-T segment of the curve. In some instances a negative T became more deeply depressed. These changes disappeared after subsidence of the pain. This evidence supports the conception that transient anginal attacks are due to myocardial ischemia, presumably due to alteration in coronary artery flow. Electrocardiograms taken during other types of paroxysmal pain (labor pains, renal and gallstone colic) did not show any changes in the T wave or S-T portion of the curves.

Nutritional Edema.—Weech and Ling discuss the relation of serum protein deficiency to various types of edema, both experimental and clinical. Attention is called to other factors and in particular to the rôle of several inorganic salts in modifying the effect of protein deficiency alone. In a series of patients suffering from nutritional edema, who were studied during both the active and the convalescent stages, it was found that when the level of serum albumin was greater than 2.9 Gm. per hundred cubic centimeters edema was never observed and that when the level fell below 2.5 Gm. per hundred cubic centimeters edema was invariably present. The correlation with total serum protein, although not so close, was sufficient to indicate a critical level for edema close to 5 Gm. per hundred cubic centimeters. Serum globulin was exceedingly variable: decreased, normal and increased values all were found in association with edema. Decreased globulin generally occurred only when the albumin was also decreased and thus was usually present in association with edema. No relation of cause and effect was considered, however, to exist between lowered globulin and edema. The results of metabolism observations on two of these patients are given. In both cases the combined administration of sodium chloride and sodium bicarbonate led to rapid gain in weight, marked increase in edema and depression of chloride excretion in the urine. In one of the patients these effects could not be reproduced after feeding of an adequate diet had resulted in a return to normal of the serum protein. The impossibility of offering an exact explanation of all the effects observed is pointed out, although it is stated that the results are in harmony with the view that the cation sodium is more intimately related to the causation of edema than the anion chloride.

Water in Epilepsy.—McQuarrie and Peeler present experimental and clinical data to show the effects of sustained pituitary antidiuresis and water drinking on mildly epileptic as contrasted with nonepileptic children. It is shown that typical grand mal seizures can be induced within twelve to forty-eight hours in the epileptic, but not in the nonepileptic subject, by giving water at the rate of from 2 to 5 cc. per kilogram of body weight hourly while maintaining effective pituitary antidiuresis. This difference in response between epileptic and nonepileptic patients may be helpful in establishing the diagnosis early in an obscure case. Under the conditions of the experiments described by the authors, dilution of the extracellular body fluids appears to be an essential factor in the induction of seizures since administration of an amount of sodium chloride just sufficient to prevent this tends to interfere with their occurrence. The results presented lend strong support to the view that the mechanism for controlling semipermeability of the brain cell membranes is inherently defective in the epileptic patient.

Journal of Comparative Psychology, Baltimore

12: 257-256 (Oct.) 1931

Additional Experiments on Homing of Carpenter- and Mining-Bees. P. Rau, Kirkwood, Mo.—p. 257.
Relative Efficacy of Free and Guided Learning When Equated in Terms of Time. R. H. Waters and Alma L. Ellis, Little Rock, Ark.—p. 263.
Continuity of Movement and Error Elimination in Stylus Maze. L. L. Mays, Chicago.—p. 279.
In Reply to Landis. M. N. Chappell, New York.—p. 289.
Effect of Incorrect Guidance on Human Maze Learning. R. H. Waters, Little Rock, Ark.—p. 293.
Studies in Individual Differences in Maze Ability: IV. Constancy of Individual Differences; Correlation Between Learning and Relearning. R. C. Tryon, San Francisco.—p. 303.
A Test of "Directional Sense" in Cats and Pigeons. R. H. Gundlach, Seattle.—p. 347.

Journal of Industrial Hygiene, Boston

13: 293-332 (Nov.) 1931

Studies in Dust Retention: III. Factors Involved in Retention of Inhaled Dusts and Fumes by Man. C. E. Brown, Boston.—p. 293.
Hypertension in Industry. E. J. Kirk, Omaha.—p. 314.
Injuries Produced in Organism by Discharge from Impulse Generator. O. R. Langworthy and W. B. Kouwenhoven, Baltimore.—p. 326.

Journal of Infectious Diseases, Chicago

49: 271-365 (Oct.) 1931

Thermophilic Micro-Organisms from Imported Canned Shallots (Onions). P. S. Prickett, Evansville, Ind.—p. 271.
Electrophoretic Study of Sterile Filtrates of Cultures of Streptococci of Scarlet Fever and Erysipelas. L. E. Shinn, Chicago.—p. 281.
Mycobacterium: Ergosterol Content of Certain Species and Effect of Ergosterol on Their Growth. P. S. Prickett and O. N. Massengale, Evansville, Ind.—p. 297.
Tinctorial Transmutations of Acid-Fast Micro-Organisms and Virulence of Tubercle Bacilli. F. Eberson and Marion A. Sweeney, San Francisco.—p. 303.
Microbic Dissociation in Brucella Group. M. S. Marshall and Dorothy Jared, San Francisco.—p. 319.
Pyrogenic Reaction to Concentrated Antipneumococcus Serums, with Respect to Certain Serum Constituents. L. D. Felton and Gladys Kaufmann, Boston.—p. 337.
*Influence of Artificial Fever on Course of Experimental Poliomyelitis. C. W. Jungeblut and N. Kopeloff, New York.—p. 348.
Purification of Cultures of Treponema Microdentium by Centrifugation. E. E. Ecker and L. A. Weed, Cleveland.—p. 355.
*Various Colonies of Hemolytic Streptococci in Scarlet Fever. Ruth Tunnicliff, Chicago.—p. 357.

Artificial Fever and Experimental Poliomyelitis.—The different types of data obtained by Jungeblut and Kopeloff are somewhat conflicting, which makes it difficult for them to draw conclusions. Within the limitations of the experimental material, it appears to be proved that noninfectious fever of considerable intensity applied during the period of incubation, but maintained only over comparatively short periods of time, is not capable of altering the course of experimental poliomyelitis in the monkey to any significant extent. The same holds true for infectious fever produced by inoculation with Trypanosoma equiperdum, when the two infections are induced simultaneously. With a poliomyelitic infection superimposed on an existing febrile trypanosomiasis there may be a distinct prolongation of the period of incubation of the poliomyelitic infection, undoubtedly indicating some attenuation of the virus. Since the latter observation is based on one monkey alone, the authors do not know how regular this occurrence is. With syphilis a definite spirocheticidal effect in vivo may apparently be obtained by febrile temperatures that cause no obvious damage to the host. As regards poliomyelitis, it would seem that the production of a sufficiently intense fever to bring about destruction of the virus in vivo is not possible within a safe zone of raised temperature.

Hemolytic Streptococci in Scarlet Fever.—During the course of scarlet fever, especially during convalescence and in complications, Tunnicliff isolated atypical hemolytic streptococci alone or associated with typical Streptococcus scarlatinae. They appeared to have dissociated from the typical, or "normal," slightly granular, conical scarlatinal colonies and differed from them by forming on heated blood agar (chocolate agar) granular or smooth convex colonies and the rough conial colonies did not change chocolate agar; the granular convex colonies turned it green, while the smooth convex colonies varied in this respect. By the opsonic test, the cocci from dissociated colonies were not opsonified like the group of streptococci specific for scarlet fever, but by subculturing they were reverted, both colonically and immunologically, to typical scarlatinal streptococci.

Military Surgeon, Washington, D. C.

69: 483-578 (Nov.) 1931

Obesity and Its Treatment. G. C. Beach.—p. 483.
Diet and Disease: Just How Much Have We Learned About Their Real Relationship? M. H. Epstein.—p. 489.
The A. R. A. in Russia. W. R. Dear.—p. 499.
Since the Days of the Empire. G. F. Lull.—p. 512.
Congenital Absence of Radius and Club Hand: Case. D. N. W. Grant. —p. 518.
School of Aviation Medicine. B. B. Warriner.—p. 522.

New England Journal of Medicine, Boston

205: 841-892 (Oct. 29) 1931

Studies in Asthma: XIV. Bronchoscopy in Asthma. F. L. Weille, Boston.—p. 848.
*Immunity Factors in Recovery from Lobar Pneumonia and Results of Specific Treatment in Type I Pneumococcus Pneumonia. F. T. Lord, Boston.—p. 854.
George W. Gay Lectures in Medical Ethics. W. H. Robey, Boston.—p. 856.

Results of Specific Treatment in Type I Pneumococcus Pneumonia.—Lord has noted that specific serum treatment of type I pneumococcus lobar pneumonia lowers the mortality when used during the first three days of the illness but is ineffective after this interval. Humoral immunity is to be regarded as an important cause of recovery from pneumococcus lobar pneumonia. The discrepancy between the small amount and inconstant presence of protective substances in the blood and the decisive nature of crisis, occasional recovery at the usual time in spite of the early appearance of protection, and the ineffectiveness of serum treatment after the third day of the disease, suggest that other factors may also be concerned in the defensive mechanism.

New Orleans Medical and Surgical Journal

84: 311-428 (Nov.) 1931

Operative Correction of Uterine Retrodisplacements. W. T. Dannreuther, New York.—p. 311.
One Thousand Cases of Uterine Fibroids in Negro Race. H. B. Aloebrock, New Orleans.—p. 317.
Radium in Treatment of Certain Diseases of Uterus. J. W. Barksdale, Jackson, Miss.—p. 326.
Uterosalpingography with Lipiodol. J. P. Wall, Jackson, Miss.—p. 329.
New Anastomosis Button for Gastro-Intestinal Surgery. J. T. Nix, New Orleans.—p. 332.
Diagnosis and Significance of Splenic Enlargement. J. B. Guthrie, New Orleans.—p. 340.
Rheumatic Fever and Rheumatic Heart Disease. T. M. McMillan and C. F. Nichols, Philadelphia.—p. 346.
Home Treatment of Tuberculosis. W. A. Toomer, Tupelo, Miss.—p. 357.
Hypertension. T. R. Beach, Ellisville, Miss.—p. 362.
Lobar Pneumonia and Its Treatment. E. L. Walker, Magee, Miss.—p. 369.
Uses of Sodium Ethyl-1 Methyl-Butyl-Barbiturate (Pentobarbital-Sodium) in Medicine and Surgery. G. F. Carroll, Biloxi, Miss.—p. 375.
Standard Treatment of Malaria (Preliminary Report). J. M. Adams, Baton Rouge, La.—p. 379.
History Taking. A. H. Little, Oxford, Miss.—p. 388.

Ohio State Medical Journal, Columbus

27: 841-920 (Nov.) 1931

Advances in Our Knowledge of Etiology and Treatment of Chronic Arthritis and Rheumatic Manifestations. W. C. Stoner, Cleveland. —p. 861.
Hysterectomy. R. B. Drury, Columbus.—p. 863.
Maternal Mortality and Morbidity in Ohio. B. H. Carroll, Toledo.—p. 865.
Some Suggestions for Better Cooperation Between Psychiatrists and Lawyers. C. E. Kiely, Cincinnati.—p. 869.
Bacteriology of One Hundred Consecutive Tonsils. C. L. Spohr, Columbus.—p. 872.
Practical Professional Problems of Rural Health Administration. E. R. Hiatt, Troy.—p. 877.
Cardiac Pain: Clinical Consideration. F. Jukes, Akron.—p. 879.

Southwestern Medicine, Phoenix, Arizona

15: 449-502 (Oct.) 1931

Effects of Liver Diet on Nervous System Symptoms in Pernicious Anemia. W. C. Menninger, Topeka, Kan.—p. 449.
Medical Jurisprudence. H. H. Clark, Denver.—p. 453.
Conservative Treatment of Cancer of Mouth and Lower Lip. J. M. Martin, Dallas, Texas.—p. 458.
Diagnosis and Management of Rectal Cancer. C. Rosser, Dallas, Texas. —p. 464.
Personal Observations of Cholecystitis. J. Vance, El Paso, Texas.—p. 467.
Brain Injuries. S. D. Swope, El Paso, Texas.—p. 470.
Hypertensive Disease. D. G. Stine, Columbia, Mo.—p. 473.
Trichinosis: Report of Cases. J. A. Rawlings, C. Awe and J. M. Rawlings, El Paso, Texas.—p. 477.
Proctologic Odds and Ends. C. Rosser, Dallas, Texas.—p. 479.
Case of Tularemia. J. L. Murphy, El Paso, Texas.—p. 481.
Oral Diagnosis: With Especial Attention to Devital Roentgen-Ray Negative Tooth. L. A. Neil, El Paso, Texas.—p. 482.
Open Reduction in Treatment of Fractures, Selection of Cases, Types and Methods. A. C. Carlson, Jerome, Ariz.—p. 484.

Yale Journal of Biology & Medicine, New Haven

4: 1-115 (Oct.) 1931

Historical Studies on Nature and Treatment of Gunshot Wounds from Fifteenth Century to Present Time. T. Billroth, Berlin. Translated by C. P. Rhoads, Springfield, Mass.—p. 3.
Acute Hemorrhagic Necrosis of Pancreas: Four Cases. R. M. Goldstein. —p. 37.
Clinical Diagnosis of Intestinal Tuberculosis. E. H. Rubin, New York. —p. 45.
Bacterial Mutations. F. D'Herelle, New Haven, Conn.—p. 55.
Preclinical Sciences and Human Biology. H. S. Burr, New Haven, Conn.—p. 63.
Blood Picture of Normal Laboratory Animals. R. A. Scarborough, San Francisco.—p. 69.

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FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Anesthesia, Manchester

3: 1-56 (Oct.) 1931

Subarachnoid Block; General Analgesia; "Spinal" Anesthesia; Respiratory Paralysis; Fallacies and Methods. W. H. Jones.—p. 3.
*System of Anesthesia for Dental Anesthetist. F. P. de Caux.—p. 22.
Premedication. S. Rowbotham.—p. 41.

System of Anesthesia for Dental Anesthetist.—De Caux believes that nitrous oxide, properly administered, is the safest anesthetic agent for all ages and conditions. It is ideal for all operations on the mouth and pharynx. It is best administered undiluted until the patient is anesthetized. Asphyxial symptoms should never be allowed to persist but should immediately be relieved by oxygen either from the air or from a cylinder. Oxygen can easily be administered by the nose without interference with the surgeon. For extensive surgical work on the mouth it is best administered by way of a tube passed through the nose into the trachea. Every opportunity should be taken to make use of premedication, especially in children.

British Journal of Experimental Pathology, London

12: 279-356 (Oct.) 1931

Serum Treatment of Lobar Pneumonia: Study in Immunology. R. R. Armstrong.—p. 279.
Mucus Secretion in Acute Experimental Inflammation of Colon, and Other Mucous Membranes of Cat: Histologic Changes. H. Florey and R. A. Webb.—p. 286.
Mechanism of Goblet-Cell Secretion in Mammal: Effects of Cyanide. H. Florey.—p. 301.
Significance of Natural Variations in Structure and Cortical Lipoid of Mouse Suprarenal. R. Whitehead.—p. 305.
Glandular Fever: II. Protozoal Nature of Experimental Disease. J. O. W. Bland.—p. 311.
Human Skin Tolerance to Diphtheria Toxin, and Immunizability. S. F. Dudley.—p. 319.
Effect of Repeated Calf Passage on Immunizing Power of Vaccine Lymph. P. A. Clearkin and D. A. Skan.—p. 322.
Note on Toxicity of Amyl-Meta-Cresol. W. A. Broom.—p. 327.
Disinfectant and Antiseptic Properties of Amyl-Meta-Cresol. C. E. Coulthard.—p. 331.
Further Observations on Qualitative Differences in Antitoxic Fractions Prepared from Same Sample of Plasma. Mollie Barr and A. T. Glenny.—p. 337.
Mechanism of Voges-Proskauer Reaction and Diacetyl Reaction for Proteins. R. A. O. O'Meara.—p. 346.

British Journal of Physical Medicine, London

6: 139-158 (Oct.) 1931

*Hyperpyrexia: New Field for Physical Therapeutics. C. A. Neymann.—p. 141.
*Some Clinical Observations on Relationships Between Chronic Rheumatism and Throat Infection. J. D. Hindley-Smith.—p. 145.
Distribution of Ultraviolet Radiation in Room. H. E. Beckett.—p. 146.
On Manipulative Treatment of Tendon Lesions. I. H. Lloyd-Williams.—p. 148.
Radiologic Diagnosis. B. Leggett.—p. 151.

Hyperpyrexia.—According to Neymann, hyperpyrexia can easily be produced by diathermy and will undoubtedly prove to be a beneficial procedure in many acute and chronic diseases. At present its value in the treatment of dementia paralytica exceeds that of any other known form of therapy. With correct technic this method of producing fever can be controlled with accuracy. It permits of dosage both in time and in quantity elements. The dangers are exceedingly slight and can be entirely overcome by proper care and attention.

Relationships Between Chronic Rheumatism and Throat Infection.—The careful analysis of approximately 500 cases in which chronic rheumatism was a prominent symptom during the last three years has led Hindley-Smith to certain conclusions. First, chronic rheumatism is a symptom and not a disease *sui generis*. In about 75 per cent of cases the causal factor is the streptococcus of the viridans and hemolyticus varieties. Of the remaining 25 per cent of cases the primary cause is due to some form of chronic infection such as bacillary dysentery and gonorrhea, when any cause has been demonstrable. The evidence indicates that in the streptococcal cases the condition begins in early childhood, usually between the ages of 3 and 6. The infection appears to begin with a primary stage of invasion in the throat, with sore throats, septic tonsils, and so on, a secondary stage with constitutional disturbances affecting the blood, heart and nervous system, beginning at the ages of 9 to 14; and later in life a tertiary stage which manifests itself as chronic rheumatism and fibrositis. There is no clearly defined interval between these stages (as, for instance, in syphilis), but each stage is always recognizably represented in each case history, and in each successive stage the throat and nasopharyngeal symptoms appear to play a decreasingly obvious but none the less active part.

British Journal of Radiology, London

4: 477-532 (Oct.) 1931

*Treatment of Granuloma Inguinale by Diathermic Fulguration: Analysis of Twenty-Two Cases. F. G. Greenwood.—p. 488.
Low Voltage Radiography. A. B. McLean.—p. 500.
Reflex Phenomena in Chronic Appendicitis. G. C. Field.—p. 504.

Treatment of Granuloma Inguinale.—Greenwood presents an analysis of twenty-two cases of granuloma inguinale in which he used diathermic fulguration. He states that this form of treatment is easy to carry out, is not attended by shock, and, if general anesthesia is given at the time of operation, the patient experiences hardly any discomfort. The average time taken to heal the ulcer in the series of cases was seventy days, the greater part of the ulcer being healed in most cases in about four or five weeks. This is a very much shorter period than that taken by the antimony tartrate treatment in most cases. There were no failures in the series. Judging from the appearance of the scar and from the one follow-up case seen, the author believes that the cure is lasting. The fact that treatment merely of the edges of the ulcer is sufficient goes to confirm the work of Castellani and Mendelson that it is not the Leishman-Donovan body, found only in smears from the ulcer but a nosoparasite which is the causative organism. It also seems to indicate very strongly that the true causative organism should be looked for in the active edges of the ulcer.

British Journal of Tuberculosis, London

25: 161-208 (Oct.) 1931

*Bovine Tuberculosis and Human Infection. D. S. Rabagliati.—p. 161.
*Similarity of Certain Tuberculous Cervical Abscesses and Branchial Cysts. H. Bailey.—p. 167.
Diagnosis of Early Pulmonary Tuberculosis. H. V. Morlock.—p. 170.
Note on Tuberculosis and Suicide. A. N. Cox.—p. 173.
American Impressions of British Tuberculosis Conference. Louise Strachan.—p. 175.

Bovine Tuberculosis.—Rabagliati suggests the following policy pending a determined attempt to eliminate tuberculosis in its entirety from herds of cattle in England, a measure perfectly feasible but at the present time beyond the hope of practical politics: 1. Encouragement of the use of and therefore the production of "certified" and grade A milks. These classes of milk, if produced under proper supervision, are practically safe. 2. Milk should be produced from cows under careful veterinary supervision. Experience shows that when cows are examined quarterly or, if possible, more frequently (though this can rarely be done in a large county) the percentage of tuberculous milk sold is exceedingly small. This supervision insures that not only are many cows with tuberculosis of the udder detected but also many animals excreting tubercle bacilli by the respiratory, alimentary and even the urinary tracts, which may be responsible for infecting the milk, though such infection may only be of intermittent character. These may easily be missed if merely bulk samples are taken. 3. The use of pasteurized milk when the source of supply cannot be properly controlled. For large cities pasteurization has undoubtedly many advantages, but in advocating it its many disadvantages must not be lost sight of, and the methods by which it is carried out ought to be much more closely supervised than is usual at the present time.

Similarity of Cervical Abscesses and Branchial Cysts.—Bailey calls attention to the fact that the physical signs of a branchial cyst and a tuberculous abscess are practically identical. The patient presents himself with a cystic swelling in the upper third of the neck, deep to the upper third of the sternocleidomastoid, coming around the anterior border of that muscle. This is the commonest location of a tuberculous abscess, and also the constant situation of a branchial cyst. The skin over-

lying the swelling may or may not be slightly inflamed. In either case this is not of assistance, for branchial cysts are subject to recurrent attacks of inflammation; indeed, the patient nearly always first presents himself with a branchial cyst thus complicated. A syringe is taken and some of the contents of the swelling aspirated. The unwary will say at once "pus," but branchial fluid and tuberculous pus in a syringe have precisely the same appearance. The fluid is sent to the bacteriologic laboratory, and the usual report in the case of a tuberculous abscess is: "No tubercle bacilli found. Cultures sterile." This report is also the most likely one to be received in the case of a sample of branchial fluid. In less than 10 per cent of cases are tubercle bacilli found in the aspirated contents of a tuberculous cervical abscess. The similarity between these two conditions is truly remarkable, and it is easy to appreciate why it is so common for a branchial cyst to be diagnosed as a tuberculous abscess, and how an erroneous diagnosis can be upheld by the authority of scientific laboratory investigation. If the following suggestions and tests are applied it is possible to segregate branchial cysts, which are comparatively rare, from tuberculous abscesses connected with the upper jugular chain, which are common: 1. Branchial cysts most often appear between 17 and 25 years of age. While their appearance may be delayed until much later, they are rarely seen before puberty. 2. On carefully palpating the sternocleidomastoid with the muscle in physiologic activity, as is occasioned when the chin is forcibly pushed against the palm of the hand, one finds that the sternocleidomastoid will be thinned and flattened over the cyst, but it is unaltered when the swelling is a tuberculous abscess. This test requires some practice before the results can be relied on. 3. If a drop or two of the aspirated fluid is placed on a glass slide, covered with a cover-slip, and examined immediately under the microscope with one-sixth power lens, the presence of numerous cholesterol crystals at once makes the diagnosis of branchial cyst certain. It is unwise, and quite unnecessary, to send the specimen to the laboratory, unless one is certain that the examination will be made at once, and one specifies that the information sought is with regard to the presence of cholesterol rather than bacteriologic characteristics. The foregoing test is so reliable that it is safe to predict that if it were applied generally the majority of branchial cysts would be correctly diagnosed as soon as they appeared. As it is, even after these tests have been applied conscientiously, a few cases escape detection. The reason for this is that therapeutic aspiration, and particularly the injection of medicated preparations, as is at present fashionable, robs branchial fluid of its characteristic cholesterol. Acute, or subacute, inflammation of the cyst sometimes has the same effect.

British Medical Journal, London

2: 787-832 (Oct. 31) 1931

*Problem of Child in Tuberculous Household. R. C. Wingfield.—p. 787.
*Broken Nose. E. W. Williams.—p. 791.
*Rôle of Pituitary in Etiology of Cancer. W. Susman.—p. 794.
*Torsion of Ovarian Cyst in Children. W. A. Steel.—p. 798.
Gangrene of Skin of Diphtheritic Origin. J. S. Anderson.—p. 800.

Problem of Child in Tuberculous Household.—Wingfield believes that the general practitioner must view the problem of the child in the tuberculous household mainly as a clinical problem; his duty is to the child and its parents rather than to the community at large. He should not have to examine all the contact children in his practice by the Mantoux reaction for evidence of infection and by the roentgen ray for evidence of lesion. He should not have to deal with these patients personally; these investigations should be made for him, and he should have a knowledge of their results. His duty is to watch and to turn his attention to the proper hygiene of the home. He must realize the danger not of exposure but of continuous exposure; that is to say, he must use every effort to sterilize the open case which is the source of contact, and to dilute the infection either by treatment or by segregation, partial or complete. Contact infants must be his especial care in this direction. He must teach the parent and the adult how by attention to a few simple hygienic rules they can minimize the danger to the children almost to the vanishing point. It is not his duty, and would be a waste of his time and injurious to his practice, if he were to say to the tuberculous mother that she must never see her child again. When the contact children of his practice reach adolescence is the time he must be most wise and wary. That is the time when the parent and child need guidance in the choice of work, mode of life and environment. That is the time when the roentgen ray will be particularly useful, for apical infiltration in childhood and adolescence, although apparently latent, always goes on to definite clinical pulmonary tuberculosis if untreated.

Broken Nose.—According to Williams, the common type of "broken nose" is due to lateral (but not backward) displacement of both nasal bones with imbrication. Treatment consists of disimpaction, free mobilization of both bones, and symmetrical molding together. No splints are needed. When the nose has been crushed, internal splinting is required to restore the profile; the author describes a convenient form of splint. Resection of the septum may be needed. When a portion of the maxilla is impacted in the antrum, access is obtained by the canine fossa route. If much damage has been caused to skin and soft parts, every effort must be made to conserve tissue, limit sepsis, and prevent adhesions.

Pituitary in Etiology of Cancer.—On the basis of the hypothesis that in cancer cases the anterior pituitary was overactive, and the posterior pituitary underactive, two patients with advanced cancer were treated by Susman with solution of pituitary alone, and five with solution of pituitary and theelin. All were placed on a diet low in carbohydrate. An epithelioma began to separate off and was enucleated after seven weeks of this treatment. The growing edge disappeared in five days. All the patients showed regressive changes in the tumors, and life appeared to be definitely prolonged.

Torsion of Ovarian Cyst in Children.—Steel reviews more than twenty-five cases of torsion of ovarian cyst in children and gives an illustrative case. Ovarian tumor, though rare, increases in frequency with the age of the child and is most commonly encountered between the ages of 10 and 14. Torsion, although very rare, is the commonest complication of these tumors. A correct diagnosis of the condition is decidedly more often the exception than the rule, in spite of the fact that a constant clinical picture is found in almost every case. The typical features present are a history of similar but less severe attacks, the sudden onset of pain, an increase of temperature and pulse rate, the palpable abdominal tumor with overlying tenderness and rigidity, and the tender cystic mass, which can be made out by rectum. The diagnosis is sometimes very difficult, the lesion for which torsion of a cyst is most often mistaken being an appendical abscess.

Journal of Anatomy, London

66: 1-156 (Oct.) 1931

Some Observations on Myelination in Human Central Nervous System. M. F. L. Keene and E. E. Hewer.—p. 1.
History of Prochordal Plate in Rabbit. Y. H. Assar.—p. 14.
Further Note on Prochordal Plate in Man. J. P. Hill and J. Florian.—p. 46.
Partial Duplication of Notochord in Human Embryo of 11 Mm. Greatest Length. T. B. Johnston.—p. 48.
Growth Changes in Bushman Mandible. L. H. Wells.—p. 58.
Craniochirido Dysostosis and Normal Skull Formation. R. W. Reid.—p. 64.
Intrapontile Part of Motor Root of Facial Nerve. E. Vernon.—p. 66.
Structure of Thoracic Inferior Vena Cava in Rabbit and in Cat, and Its Functional Significance. K. J. Franklin.—p. 76.
Constitution of Ligamentum Cruciatum Cruris. T. T. Stamm.—p. 80.
Secondary Os Calcis. J. Mercer.—p. 84.
Circumaortic Venous Rings. P. N. B. Odgers.—p. 93.
Paired Oviducts in Fowl. F. A. E. Crew.—p. 100.
Development of Hyoid Bar and Rays in Plagiostomi. F. H. Edgeworth.—p. 104.
Craniometric Memoirs: IV. Horizontal Zones of Facial Norma in Modern and Fossil Man. J. Cameron.—p. 114.
Note on Relative Lengths of First and Second Toes of Human Foot. B. M. Skinner.—p. 123.

Medical Journal of Australia, Sydney

2: 405-436 (Oct. 3) 1931

*Surgical Treatment of Constipation. H. C. Trumble.—p. 405.
*Hodgkin's Disease: A Treatise. L. Uts and Leila Keatinge.—p. 412.

Surgical Treatment of Constipation.—Trumble believes that it is possible that section of the hypogastric nerve alone would be sufficient to permit of relaxation of the sphincters and

to cure some patients with Hirschsprung's disease, but until more is known about the subject it would probably be wise to adopt a more radical procedure. The simplest way to do this is to divide the lumbar splanchnic nerves just proximal to the inferior mesenteric ganglion. The author gives reports of three cases in which this was done with satisfactory results.

Hodgkin's Disease.—According to Utz and Keatinge, tuberculous lymphadenitis, which is so often mistaken for Hodgkin's disease, can be differentiated by serologic tests in children and by biopsy in adults. The histologic appearances in the tuberculous lymph nodes are not in any way similar to those found in Hodgkin's disease. True splenic anemia can be identified clinically, as a rule by the absence of palpable abdominal lymph nodes, by the absence of ascites or jaundice, or many of the pressure symptoms directly due to the presence of enlarged lymph nodes in Hodgkin's disease. To differentiate Gaucher's disease, which is incidentally often associated with enlarged superficial nodes, is a different matter. The familial occurrence of Gaucher's disease is practically the only guide short of biopsy of the nodes, which, however, may also demonstrate some resemblance to Hodgkin's disease. In spite of all that has been written about the differentiation of lymphosarcoma from Hodgkin's disease, the authors are inclined to agree with Ewing by stating that the lymphocytoma type of lymphosarcoma in which the lymphocyte and not the endothelial cell is proliferated can be differentiated at a glance by microscopic examination. But when the endothelial elements of lymph nodes proliferate to produce a so-called lymphosarcoma of the endothelial type, differentiation either clinically or on histologic grounds is practically impossible. In differentiation one relies solely on the appearance of the Dorothy Reed cells, but a great number of cases of Hodgkin's disease are then classified as lymphosarcoma. Clinical differentiation between these two diseases is well nigh impossible. Leukemia can be identified in practically all instances by the blood picture and, as the pseudoleukemia of Sternberg is still a disease without a clinical entity, differentiation is impossible.

South African M. Assn. Journal, Cape Town

5: 617-656 (Oct. 10) 1931

Constipation. S. F. Silberbauer.—p. 619.
Constipation. G. J. Joubert.—p. 623.

Tubercle, London

12: 49-96 (Nov.) 1931

Sanocrysin Treatment. V. S. Christensen.—p. 49.
Pathogenic Properties of BCG. Critical Review of Experiments of K. T. Sasano and E. M. Medlar. A. Boquet.—p. 62.

National Medical Journal of China, Shanghai

17: 393-686 (Aug.-Oct.) 1931

Amebic Abscess of Liver: Forty-Eight Cases with Particular Attention to Treatment. S. M. Chen, G. W. van Gorder and Y. K. Yuan.—p. 393.
Endamoeba Histolytica Infection in North China: One Thousand Positive Cases. S. M. Tao.—p. 412.
*Lymphatic Reaction in Experimental Trypanosomiasis. C. H. Hu.—p. 435.
Attempt to Immunize Hamsters Against Kala-Azar. T. J. Kurotchkin.—p. 458.
Filariasis in China with Especial Reference to Its Distribution and Transmission. L. Feng.—p. 464.
Historical Notes on Fasciolopsis Buski (Lankester, 1857) Odhner, 1902. O. K. Khaw.—p. 473.
Bertiella Elongata Bourquin, 1905, and Bertiella Studeri Blanchard, 1891, from Flying Lemurs in Philippine Islands. H. J. Chu.—p. 488.
Larvae and Pupae of North China Species of Anopheles: Their Structure and Breeding Habits. L. C. Feng.—p. 493.
Observations on Incidence of Anopheles in Rural Area Outside Peiping and on Conditions of Anopheles Breeding. C. P. Yang.—p. 513.
Mycologic Study of Tinea of Glabrous Skin. T. J. Kurotchkin and F. K. Chen.—p. 521.
Tinea Favosa in Peiping. F. K. Chen, T. J. Kurotchkin and C. K. Hu.—p. 529.
*Tinea of Nails in Peiping. T. J. Kurotchkin and T. L. Ch'in.—p. 534.
Histologic Reactions in Skin Due to Ectoparasites. R. Hoeppli and L. C. Feng.—p. 541.
*Histologic Changes in Digestive Tract of Vertebrates Due to Parasitic Worms. R. Hoeppli and H. F. Hsü.—p. 557.
Parasitic Nematodes Mostly from Snakes Collected in China. H. F. Hsü and R. Hoeppli.—p. 567.
Action of Esophageal Glands of Parasitic Nematodes. R. Hoeppli and L. C. Feng.—p. 589.
Transmission of Kala-Azar to Hamsters (Cricetulus Griseus) by Feeding Them with Infected Carcasses. O. K. Khaw.—p. 599.
Early Case of Kala-Azar, Possibly Oral Infection in Laboratory. H. L. Chung.—p. 617.
Survey of Peiping Latrines for Intestinal Parasites. O. K. Khaw.—p. 622.
Treatment of Worm Diseases with Chinese Drugs: From the Pen Ts'ao Kang Mu with Notes. B. E. Read.—p. 644.
Extracts from Some Old Chinese Medical Books on Worm Infections. H. J. Chu and I. H. Ch'iang.—p. 655.

Lymphatic Reaction in Trypanosomiasis.—White rats experimentally infected with Trypanosoma brucei were studied histologically by Hu, at different stages of infection. It was found that this infection produces a massive hyperplasia of the reticulo-endothelial system, increased intramedullary and extramedullary erythropoiesis and myelopoiesis and a striking hyperplasia of the lymphoid tissue. There is no evidence, however, to show that one element can be transformed into the other. The lymphatic hyperplasia, which takes place chiefly in the spleen and the lymph nodes, consists of a great increase in number of large and medium sized lymphoblasts which, in the early stage of infection seem to be formed directly from certain small lymphoid cells in the lymphoid tissue of these organs. These lymphoblasts, once formed, may either undergo rapid cell division, forming other lymphoblasts, or become transformed into plasma cells. Although the lymphoblasts of the germinal centers and the rest of the lymphoid tissue participate in this generalized hyperplasia, the large and medium sized lymphocytes and a certain number of the small lymphoid cells do not undergo significant change. Especially striking are the small lymphoid cells of the thymus, all of which remain practically unaltered in the whole course of infection. The failure of these cells to take part in this reaction is interpreted by the assumption that they are true small mature lymphocytes which, with the ordinary histologic methods, are indistinguishable from the small primitive cells capable of forming larger lymphoblasts.

Tinea of Nails.—Kurotchkin and Ch'in report that a study of eighteen cases of onychomycosis revealed two clinical forms of the disease. The most common form was characterized as a rule by considerably thickened and brittle nails which were also either ridged or otherwise deformed. In the second form the nails were smooth and had an abnormally dull white color, characteristic of leukonychia. In the later type of case the fungus was found in abundance in the scrapings from the surface of the nail. Three species of Epidermophyton were isolated from thirteen cases. Cultural examination of the remaining five cases was negative for fungi. Epidermophyton rubrum was present nine times among the thirteen cases. This fungus was also responsible for the infection in the two cases with leukonychia. It was observed that onychomycosis is a secondary infection in the majority of cases. It may develop as a result of the extension of the infection from cutaneous mycotic lesions such as occur in tinea of the feet and hands. It may also accompany tinea cruris, in which case infection of the nails is probably due to self inoculation. This conclusion is based on the fact that in cases of coexisting mycoses the same organism has regularly been isolated both from the nails and from the skin.

Changes in Digestive Tract Due to Parasitic Worms.—Of the various histologic changes in the intestinal tract of vertebrates due to parasitic worms, the following are briefly described by Hoeppli and Hsü: superficial lesions of the mucosa due to mechanical action of organs like suckers, rostellum, and buccal capsule; changes mechanically produced in the glands, and lesions of the deeper layers of the intestinal and stomach wall. The changes of the first group are very similar in principle; an inflammatory reaction and ulcer formation occur usually only in cases in which the parasite anchors in one position for a long time. The mechanically produced changes of the glands consist in a torsion and widening, which vary from a very slight degree (Strongyloides species) to a very high degree (Tetrameres species and Cotylaspis species). Lesions of the deeper layers are represented by nodules of different structure, ulceration which depends for its histologic picture on the development of the esophageal glands, and tunnel formation (Spiroxys japonica).

Paris Médical

2: 345-356 (Oct. 24) 1931

Vernes Resorcinol Reaction in Nontuberculous Diseases. C. Gernez. —p. 345.
pH of the Urine in Various Psychoses. Laignel-Lavastine, R. Cornelius and G. d'Henecqueville.—p. 348.
*Pain Syndrome of Fifth Lumbar Vertebra in Young Women. D. C. Roederer.—p. 354.

Pain Syndrome of Fifth Lumbar Vertebra.—For several years, Roederer has been noting a pain syndrome, not accompanied by contracture, which affects the region of the fifth lumbar vertebra in young women at the end of puberty. These young women range in age from 13 to 25 years (the oldest still have the exterior habitus of adolescents). The pain is fixed and constant, never very acute, but annoying by its persistence. Some patients complain simply of inconvenience; there is sometimes a sensation of burning or pricking and almost always a sensation of heaviness. The pains are spontaneous, with periods of eclipse. A prolonged upright or sitting position sometimes brings on the symptoms. The pain does not radiate to the buttock, thigh, groins or organs in the true pelvis. The menses usually aggravate the condition. The evolution of the syndrome is irregular; several weeks of latency are often followed by a reappearance of symptoms without apparent cause. Generally after from twelve to eighteen months the pains disappear either gradually or suddenly. The recovery seems absolute; a follow-up of old cases proved that it is permanent. The syndrome resembles that of painful occult spina bifida of the fifth lumbar vertebra reported by other workers. However, the author's syndrome appears in women only, while the related syndrome occurs in both sexes. Palpation localizes a painful spot in the region of the spinous process of the fifth lumbar and the first sacral vertebra; but the sensitive region is sometimes more extensive and includes the articular processes between the fourth and fifth lumbar vertebrae and even the transverse processes of the sacral vertebrae. However, the spinous process of the fifth lumbar or the first sacral vertebra always responds with the maximum of pain on pressure. The diagnosis of the syndrome is very delicate and is sometimes uncertain for weeks and even months; there is no indication of Pott's disease or sacral osteitis, and the roentgenograms are negative. The therapy is only palliative. The author recommends rest, with local and general sedatives. He believes this syndrome is sufficiently characteristic to be designated as an entity.

Presse Médicale, Paris

39: 1533-1556 (Oct. 21) 1931

*Mean Hypertension During Exertion: Cardiac Function. H. Vaquez, D. M. Gomez and R. J. Lajoie.—p. 1533.
Gastrectomy and Gastro-Enterostomy in Treatment of Ulcer. Bergeret and Caroli.—p. 1535.
Criteria of Healing in Gastric and Duodenal Ulcers. R. A. Gutmann. —p. 1537.
Action of Insulin in Ulcerous Cancers of Skin. S. F. Gomes da Costa. —p. 1541.

Mean Hypertension During Exertion.—Vaquez and his co-workers believe their researches demonstrate that the mean arterial pressure constitutes a true physiologic constant. In a previous paper (*Presse médicale* **39**:1309 [Sept. 5] 1931; abstr. THE JOURNAL, November 7, p. 1419), Vaquez and Gomez described the method for the oscillometric determination of the mean blood pressure. Subsequent researches led to the following conclusions: In well compensated cardiac disease the mean pressure is similar to what it is under normal conditions; that is, following exertion there is no change or very slight change in the mean pressure. It is otherwise when cardiac insufficiency is present and the right ventricle is affected. An elevation of the mean pressure is not due to acceleration of the pulse, since there is often acceleration of the pulse in the compensated condition. In dextrocardiac insufficiency, moreover, the elevated mean pressure subsequent to exertion returns but slowly to its former level. In persons with compensated cardiac disease an elevation of the mean arterial pressure following exertion may be a premonitory sign of approaching cardiac failure. The authors believe that a consideration of the extreme pressures is not sufficient. To determine the exact functional capacity of the heart, the mean arterial pressure should be ascertained both in a state of rest and in a state of action.

Annali Italiani di Chirurgia, Naples

10: 1005-1109 (Sept. 30) 1931

Bilobate Stomach: Autoplastic Reconstruction; Recovery. G. Pascale. —p. 1008.
Possibility of Contaminating Gloves and Tissues During Surgical Interventions. L. Torraca and M. Romeo.—p. 1027.
*Mechanism of Action of Hypertonic Solutions of Sodium Chloride. A. G. Chiariello.—p. 1047.
*Injections of Calcium Salts into Tissues Adjacent to Fractures, Under Pathologic Conditions. S. Rollo.—p. 1059.
Uronephrosis and Tuberculous Infection. G. B. Cengiarotti and E. Nalin. —p. 1069.

Action of Hypertonic Solutions of Sodium Chloride.—Chiariello studied the effects of intravenous injections of hypertonic solutions of sodium chloride on dogs in which both ureters were ligated experimentally. He observed that the dogs so treated and doomed to die survived longer than the controls that were not so treated. Such survival amounted, on the average, to 21.8 hours. It is difficult to explain the mechanism of the action, but the author is inclined to assume a direct antitoxic action of the hypertonic solutions.

Injections of Calcium Salts into Tissues Adjacent to Fractures, Under Pathologic Conditions.—Rollo reports that, from his experiments on animals (rabbits and guinea-pigs), it appears that injections of calcium glycerophosphate into the tissues immediately adjacent to a fracture serve to stimulate the focus to greater activity. They cause the early and abundant formation of new connective tissue and favor the ossification of the bone. While the second fact was established by previous experiments on sites of fractures under ordinary physiologic conditions, the first is proved especially in cases of partial diaphyseal resection and the interposition of muscle tissue between the bone fragments, in which (through parvicellular infiltration and the ample formation of new connective tissue) the destruction and replacement of the muscle tissue, and the formation of callus, inducing ossification, were facilitated. In the controls the interposed muscle tissue, preserving its integrity longer, impeded the normal evolution of the callus.

Giornale di Clinica Medica, Parma

12: 1039-1102 (Oct. 10) 1931

*Pulmonary Hyperventilation: Behavior of Lactic Acid in Blood and Alkali Reserve. G. Lucchi and B. Manfredini.—p. 1042.
Effects of Pulmonary Tuberculosis and of Artificial Pneumothorax on Glutathione of Blood. G. Borsalino.—p. 1057.

Pulmonary Hyperventilation; Behavior of Lactic Acid in Blood and Alkali Reserve.—Lucchi and Manfredini, continuing their researches on pulmonary hyperventilation, studied in twenty subjects the behavior of lactic acid of the blood and of the alkali reserve in voluntary hyperpnea. They found a notable and almost constant diminution of the alkali reserve and an increase of the lactic acid, both being more marked the more intense and the more extensive the muscular spasms were. The authors consider that the diminution of the alkali reserve is due partly to an increased elimination of carbon dioxide through the respiratory passages and partly to the hyperlacticemia provoked by the effort of the musculature and, above all, by the muscular spasms.

Policlinico, Rome

38: 477-532 (Oct. 1) 1931. Medical Section

*Experimental and Clinical Data on Prophylactic and Therapeutic Value of Antidiphtheritic Serum. T. Pontano.—p. 477.
Polycystic Kidney. R. Rossoni.—p. 498.
Existence of Endocarditis Due to Bacterium Coli-Commune. G. Borruso. —p. 511.
Tuberculosis of Spleen with Large Caseous Nodes. P. Mariconda.—p. 524.

Prophylactic and Therapeutic Value of Antidiphtheritic Serum.—Pontano studies the diphtheria problem in its three fundamental aspects: experimental, statistical and clinical. Experiments on the guinea-pig have led to wrong interpretations of human diphtheria. The prophylactic and therapeutic experiments with serums on the guinea-pig show only the prophylactic and noncurative value of the serum. The author took up the experiment by infecting the guinea-pig with bacilli and not merely intoxicating it with a toxin. He confirms the prophylactic value against the bacterial infection, both as to

local manifestations and as to toxemia. He accords the serum no action on the established disease as regards either the local infection or the toxemia. An unbiased examination of the statistics led him to conclude that the reduction in the mortality from diphtheria is due to other causes than to the use of serotherapy. Clinical evidence in a large number of personal cases does not point to a curative action of the serum. In grave cases the mortality was the highest when the serum was employed. The serum does not have any effect on the local lesions. With serum, the mortality from diphtheria is high when the seat of the disease is laryngeal. In the ordinary cases of the disease the mortality is the same without serum as with serum.

Revista Española de Medicina y Cirugia, Barcelona

14: 507-562 (Oct.) 1931. Partial Index

*Action of Histamine on Hydrogen Ion Concentration and Alkali Reserve. V. González Calvo and J. Martinez Bruna.—p. 508.

Action of Histamine on Hydrogen Ion Concentration and Alkali Reserve.—González Calvo and Martinez Bruna made determinations of the hydrogen ion concentration and the alkali reserve in patients with several pathologic conditions, either during rest or during work, and before and after eating, to ascertain what the modifications of the acid-base equilibrium are under the influence of histamine. One of the patients had diabetes. The work was preceded by determinations of the same nature in rabbits. The dose of histamine given to man was 1 mg. administered subcutaneously. From their observations the authors reach the following conclusions: Histamine has a marked action on the hydrogen ion concentration and on the alkali reserve both of man and of rabbits. Because the mechanism controlling the acid-base equilibrium is better developed in man than in rabbits, thus permitting in the former a partial inhibition of the action of histamine, the changes in the hydrogen ion concentration and in the alkali reserve under the influence of histamine are more marked in rabbits than in man. They are of a transient nature, lasting no longer than an hour and a half, and are manifested in rabbits by the appearance of alkalosis. The processes of digestion, muscular work and the like cause marked changes in the acid-base equilibrium, and these changes are more marked when the determinations of hydrogen ion concentration and alkali reserve are made simultaneously. The action of histamine varies according to the conditions of the given individual, although histamine affects more intensely the hydrogen ion concentration than the alkali reserve. The authors cannot as yet give a conclusive statement on the action of histamine on the acid-base equilibrium of diabetic patients, since the number of observations is not sufficient (only one diabetic patient was observed by them). Further determinations of the same nature in diabetic patients are planned.

Semana Médica, Buenos Aires

38: 1177-1240 (Oct. 15) 1931. Partial Index

*Cancerous Degeneration of Tubuloracemose Gland During Evolution of Chronic Erosive Hypertrophic Cervicitis. E. A. Votta.—p. 1184.
Prolapse of Umbilical Cord Followed by Delivery of Living Child. S. N. Berra.—p. 1193.
*Benign Acute Lymphocytic Meningitis Simulating Tuberculous Meningitis. J. Silberstein.—p. 1194.
Treatment of Cranial Trauma and Its Sequelae. M. Balado.—p. 1204.
Surgical Treatment of Cicatricial Stenosis of Esophagus. G. Suárez Aguirre.—p. 1217.

Cancerous Degeneration of Tubuloracemose Gland of Cervix Uteri.—The most interesting fact in Votta's case is the important information given by the biopsy, done in a patient with chronic erosive hypertrophic cervicitis, by which the presence of a malignant degeneration of a tubuloracemose gland of the cervix uteri was discovered and treated early by exeresis of the cervix, containing the degenerating tissues, and by radium therapy. Clinical symptoms of the presence of a malignant process in evolution had not been previously discovered. The patient is observed at frequent intervals for recurrences, which up to the present have not appeared. The microscopic characteristics of the tumor, a plasmodial epithelioma, are given in detail in illustrations. The neoplastic degeneration of the glandular epithelium in the author's case supports the theory of the common glandular origin of epitheliomas of the cervix uteri.

Lymphocytic Meningitis Simulating Tuberculous Meningitis.—Silberstein states that there is a type of epidemic benign meningitis in which the differential diagnosis from certain diseases or conditions, such as syphilis, epidemic encephalitis, trauma, acute poliomyelitis or some other disturbances, is easy. The disease attacks adults (usually young men). It simulates so closely tuberculous meningitis that a differential diagnosis between these two forms of meningitis is difficult. The cerebrospinal fluid in this type of meningitis contains a large number of lymphocytes. Its sediment is negative for tubercle bacilli and when inoculated into a guinea-pig gives negative results. The disease follows an evolution to spontaneous recovery without leaving any sequelae, an occurrence which is rarely observed in cases of tuberculous meningitis. The author states that the performance of the biologic test and the isolation and cultures of the causal bacteria are necessary to include this new entity of meningitis in the pathology of the nervous diseases.

Deutsches Archiv für Klinische Medizin, Leipzig

171: 431-594 (Sept. 21) 1931

*Normal Size and Form of Heart in Man. F. Moritz.—p. 431.
Increase of Total Amount of Blood in Patients with Cardiac Disease. K. Nordmeyer.—p. 477.
Healing Tendency of Duodenal Ulcer. K. Goette and H. Peters.—p. 486.
*New Treatment of Typhoid Bacillus Carriers. N. Onodera, G. Murakawa and S. Liu.—p. 503.
Studies on Metabolism of Blood Pigment. L. Heilmeyer.—p. 515.
Free and Combined Amino Nitrogen in Deproteinized Blood and Tissue Under Normal and Pathologic Conditions. E. Becher and E. Herrmann. —p. 529.
Idem. E. Becher and E. Herrmann.—p. 547.
Significance of Sternal Puncture in Anemias and Modification of Bone Marrow by Liver Treatment. I. Barta.—p. 565.
Clinical Significance of Deviation of Axis to Left in Electrocardiogram on Basis of After-Examinations. C. Korth and S. H. Proger.—p. 578.

Normal Size and Form of Heart in Man.—In the introduction, Moritz points out that at necropsy the determination of the dimensions of the heart is usually limited to measuring the thickness of the walls, the median length and the basal circumference of the ventricles, and to weighing the heart. In the main part of the article he aims to show what size of the heart can still be considered normal or is already abnormal. He considers as the best method the determination of the correlations of the heart measurements to the other body measurements. The size of the heart is determined by orthodiagraphy. The author reaches the conclusion that, for the determination of the normality of the size of the heart, the body height is the best correlative.

New Treatment of Typhoid Bacillus Carriers.—Since the typhoid bacilli in carriers usually lodge in the biliary tract and since halogen compounds have a bactericidal effect, Onodera and his associates treated seven typhoid bacilli carriers by giving intravenous injections of tetiothalein sodium and after a certain time the region of the gallbladder was irradiated with roentgen rays. Of seven patients who were treated in this manner, three became free from bacilli (bile and feces), two remained free from bacilli for a month following the treatment, and in the other patients, who are still under clinical observation, the treatment was without effect. Considering the ineffectiveness of the other therapeutic measures that have been recommended for bacillus carriers, the authors think that since their method produces favorable results in some cases it justifies further investigation.

Klinische Wochenschrift, Berlin

10: 1977-2024 (Oct. 24) 1931

Metabolism During Bodily Exertion. E. Simonson.—p. 1977.
Clinical Significance of Degenerative State. Berta Ascher.—p. 1981.
Modification of Smallpox Diagnosis According to Paul. W. Jadassohn, H. Schläpfer and L. Braun.—p. 1985.
Examination and Estimation of Ferment Preparations. C. A. Rojahn and J. A. Müller.—p. 1987.
Biochemistry of Hemolytic Icterus. A. Brock and Anna Joffe.—p. 1990.
*Function of Stomach Following Removal of Antrum Pylori. C. J. Johnson.—p. 1991.

Use of Citrated Extracts for Serodiagnosis of Syphilis by Means of Flocculation. H. Sachs and E. Witebsky.—p. 1993.
Milk Hygiene. M. Klimmer.—p. 1994.
*Aspects of Diabetes with Insulin Resistance. F. Serio.—p. 1998.
Action of Corrosive Mercuric Chloride. W. Heubner.—p. 1999.
*Intracutaneous Injection and Basal Metabolism. W. Crecelius.—p. 1999.
Modification of Bactericidal Power of Blood by Mineral Salts. L. K. Wolff.—p. 2000.
Idem. H. G. Scholtz.—p. 2000.
Ketonuria: Test of Partial Function of Liver. H. Staub and P. Clerc. —p. 2001.
Water Metabolism During Valvular Defects. H. Elias and J. Goldstein. —p. 2002.
Glycolability and Its Clinical Manifestation. G. Fanconi.—p. 2002.

Function of Stomach Following Removal of Antrum Pylori.—Johnson performed on dogs resection of the antrum pylori and gastro-enterostomy, and, immediately below, a duodenal fistula was made. It was found that the secretion of such a stomach is reduced, especially if porridge and soups are fed; but even if meat, bread and vegetables are given, the gastric secretion is reduced. If soups and porridge are fed, the stomach retains the food only for a short time, but solid foods are retained much longer. As soon as the food enters the duodenum there takes place, even under these unphysiologic conditions, a complete mixture with the duodenal secretions, and thus the hydrochloric acid is largely neutralized.

Aspects of Diabetes with Insulin Resistance.—Serio states that patients with the form of diabetes which is resistant to insulin usually appear well nourished, have only slight acidosis and are influenceable only slightly by dietetic measures. He then describes the clinical history of such a patient. Since dietary measures as well as insulin therapy failed in their effect and since the patient showed slight symptoms of hyperthyroidism, an antithyroidal preparation was administered in increasing quantities. After forty days of this medication the insulin resistance had completely disappeared, so that 14 units of insulin was now sufficient to reduce the glycemia considerably and even to produce hypoglycemic symptoms. The sugar content of the blood during fasting became normal and could be kept in normal limits in spite of a free diet and of tolerance tests, even after the treatment had been discontinued. The renal elimination of sugar continued. This was probably due to a renal factor, which became evident after the hyperglycemia had disappeared.

Intracutaneous Injection and Basal Metabolism.—Crecelius describes experiments which prove that intracutaneous injection, that is, irritation of the sympathetic nervous system, causes changes in the basal metabolism, whereas if the injection is made subcutaneously or intramuscularly there is no such effect. However, not all persons react in the same manner. To what causes it may be ascribed that in some persons there is an increase in the basal metabolism while in others there is a decrease has not been detected as yet. A careful control of the blood pictures gave no explanation, since a certain uniformity was not detectable.

Medizinische Klinik, Berlin

27: 1445-1482 (Oct. 2) 1931. Partial Index

Etiology and Clinical Aspects of Megaduodenum. V. Schmieden and Kraas.—p. 1445.
Expert Testimony on Diabetes. H. Strauss.—p. 1450.
*Membranous Colitis a Disappearing Disease. I. Boas.—p. 1451.
*Apple Diet and Intestinal Flora. W. Schreiber.—p. 1452.
Action of Insulin on Gastric Function and Its Diagnostic and Therapeutic Significance. H. Heller.—p. 1454.
Investigations on Liver Function in Chronic Stage of Epidemic Encephalitis. L. Hess and J. Goldstein.—p. 1461.
Free Organ Transplantation in Animal Experiments. W. Reiprich.—p. 1461.

Membranous Colitis a Disappearing Disease.—Boas points out that membranous colitis, which thirty years ago was one of the most discussed intestinal disorders, in recent years has hardly been mentioned, and he is convinced that the reason for this is the decreased frequency of the disease. In the last decades of the last century, when the incidence of membranous colitis was greatest, the various forms of colitis were usually treated by medicated and especially by astringent enemas. Modern medicine has done away with the habitual enema treatment and particularly with the medicated and astringent enemas, and the author thinks that membranous colitis has decreased in the same ratio as the use of enemas. Another reason why he considers enemas and especially medicated ones as the etiologic factor of membranous colitis is that in the rare cases of membranous colitis which came under his observation in recent years the anamnesis always revealed the habitual use of enemas. When the enemas were discontinued and a dietary treatment was introduced instead, the patients no longer complained of the discharge of membranes. On the basis of past experiences, the author concludes that the cause of the membrane formation is a simple colitis, for the treatment of which unreasonable methods, such as enemas, were prescribed. In this manner a simple mucous colitis developed into a membranous colitis. Since colitis is no longer treated in this manner, and since likewise the use of cathartics has diminished, membranous colitis has almost disappeared.

Apple Diet and Intestinal Flora.—Schreiber shows that in acute and catarrhal intestinal diseases, such as Flexner's dysentery, paratyphoid B and the common dyspepsias, an apple diet causes a change in the intestinal flora, which manifests itself in a considerable increase in the coli bacteria and in a decrease in the pathogenic intestinal flora. At the same time, the clinical manifestations disappear. The virulence of the coli strains neither increases nor changes as the result of the treatment, so that a predisposition for the disease may persist in spite of the clinical cure.

Münchener medizinische Wochenschrift, Munich

78: 1731-1772 (Oct. 9) 1931

Treatment of Chronic Diarrhea. P. Morawitz.—p. 1731.
Investigations on Hypotensive Remedies. J. Eversmann.—p. 1734.
Pathogenesis, Prophylaxis and Therapy of Thrombosis and Thrombophlebitis. Eichenlaub.—p. 1737.
*Intramuscular Calcium Therapy (Calcium Gluconate) in Pulmonary Tuberculosis. E. Undritz.—p. 1741.
Present Status of Cancer Research. Borst.—p. 1745.
Recognition of Poisoning on Corpses. K. Meixner.—p. 1750.
Supplementary Catheter for Trocar Especially in Ascites. S. Munter. —p. 1753.
Proposition for Effective Treatment of Recent Urethral Gonorrhea in Women and for Prevention of Ascending Gonorrhea. A. Sack and R. Amerbach.—p. 1753.
*Pathogenesis and Therapy of Leukorrhea. E. Pulay.—p. 1755.
How Much Latin and Greek the Medical Student Should Know. S. Schwarz.—p. 1755.
Observations on Nicotine Abstinence. H. Crickeli.—p. 1756.

Intramuscular Calcium Therapy in Pulmonary Tuberculosis.—Undritz employed intramuscular injections of calcium gluconate in sixty patients with tuberculosis. The injections are given every other day, alternating into the right and left gluteal muscles. In some cases the injections can be interrupted for some time, and later another series may be given. Intravenous injections of calcium gluconate are advisable in cases of hemorrhage, and a prolonged intramuscular administration may be followed by a series of intravenous injections. The author gives a tabular report, showing the results of the treatment in sixty cases, and a detailed report of three cases. He concludes that intramuscular calcium therapy is advisable in all forms of pulmonary tuberculosis, but in patients with high temperature and poor general condition the injections of calcium gluconate should be postponed until the active manifestations have somewhat subsided and the general condition has been improved by camphor therapy. Especially suitable for parenteral calcium therapy are patients with pleural exudation, and also patients who receive pneumothorax treatment, for in these cases the inhibiting action of calcium on the exudation is of especial value. A prophylactic administration of calcium is advisable from one to two weeks before the pneumothorax is induced. In the summary the author stresses that the calcium administration cannot be considered as a causal therapy and that not all patients are benefited by it. However, he considers it a valuable adjuvant. Its efficacy is due to transmineralization of the organism; that is, it does not form calcium deposits, but, in passing through the organism, it displays pharmacodynamic actions, such as increasing the phagocytosis and checking the inflammation and exudation.

Pathogenesis and Therapy of Leukorrhea.—Pulay's observations indicate that leukorrhea is a manifestation of avitaminosis. Clinically considered, leukorrhea belongs to the group of seborrheal eczema, urticaria, chronic rhinitis and hay

fever. In many cases of leukorrhea the anamnesis reveals that disorders of the skin existed in earlier years. Since it is possible to counteract seborrheal eczemas in children by administration of vitamin A, the author tried vitamin treatment in cases of leukorrhea. In some of the cases, administration of vitamins A and D effected a rapid improvement, but other cases were at first refractory. In the majority of the cases belonging to the latter group, severe seborrhea existed. Soon after a protein-free diet was instituted, these cases yielded to vitamin therapy. In order to determine the correlation between these factors, the author studied the blood chemistry of these patients and detected a reduced alkali reserve, acidosis and low magnesium content. In patients in whom the cholesterol content was normal or somewhat reduced, the vitamin treatment became rapidly effective; however, in the patients with severe seborrhea, in whom vitamin therapy was at first ineffective, the cholesterol content of the blood was considerably increased. Only after the cholesteremia had been counteracted by the proper dietary treatment did the vitamins become effective. These observations indicate the significance of the metabolic conditions in the pathogenesis of leukorrhea and show that the leukorrhea problem is largely dietary.

Wiener klinische Wochenschrift, Vienna

44: 1297-1328 (Oct. 16) 1931

Cerebral Attacks and Angiospasm in Persons with Hypertension. J. Pal. —p. 1297.
*Unnoticed Biologic Law and Its Significance for Research and Practice. J. Wilder.—p. 1299.
Ascending Thrombosis of Vena Cava Inferior. H. Dibold.—p. 1304.
Antipyrine Abuse for Sixteen Years: Case. W. Raab.—p. 1306.
Late Tetanus from Blunt Trauma More Than Fourteen Years After War Injury. W. Ernst.—p. 1308.
Disturbances in Anesthesia. E. Garzo.—p. 1310.
Carcinoma of Uterus with Especial Consideration of Early Diagnosis. P. Werner.—p. 1312.
Tumors of Jaws with Especial Consideration of Early Diagnosis. H. Pichler.—p. 1315.
Diagnosis of Acute Coronary Occlusion and Conditions for Which It Might Be Mistaken. D. Scherf.—p. 1318.
After-Treatment Following Operations on Hemorrhoids and on Varicose Veins. M. Jerusalem.—p. 1319.

Unnoticed Biologic Law and Its Significance for Research and Practice.—Wilder describes the results of his clinical experimental researches on the autonomic nervous system. He investigated the Eppinger-Hess theory of vagotony. The usual doses of atropine, epinephrine and pilocarpine were administered subcutaneously, and especial attention was given to the pulse rate and the blood pressure. On the basis of his observations he concludes that it is incorrect to assert that in the individual the usual manner of testing reveals a characteristic reaction to atropine, epinephrine and pilocarpine. There are differences in the quality and even in the types (vagotonic and sympathicotonic) of the reactions in the same person. In all types of experiments it was found that in about 75 per cent of the cases the difference in the outcome of the tests concurred with a difference in the initial values of pulse rate and blood pressure. It was observed that the higher the initial values the less the tendency to increase but the greater the tendency to decrease. If the initial value is high, the increase is slight but the decrease is marked; on the other hand, if the initial value is low the increase is great, while the falling off is slight. This is the biologic law to which the author has reference, and he terms it the law of the initial value (ausgangswertgesetz). The already existing state of irritation influences the irritability; that is, the higher the existing irritation or degree of activity, the lesser the responsiveness to increasing influences and the greater to inhibiting influences. In the second part of the article the author discusses the practical significance of this law. It explains many apparent contradictions; for instance, that the same person may react differently to the same dose of the same pharmaceutic preparation, or that the pulse rate reacts differently from the blood pressure, or that the reaction does not correspond to the dose. Knowledge of this law is also important for therapeutic measures, especially in spheres in which the vagosympathetic antagonism is involved. The author discusses the basal, sugar and calcium metabolism; also diuresis, temperature, iodine and the thyroid, the pharmacodynamic actions of cardiac remedies, the reactions of the pupils, the uterus, the stomach and the mechanism of perspiration.

Zentralblatt für Gynäkologie, Leipzig

55: 2985-3040 (Oct. 10) 1931

Biologic Action of Rays of Various Wavelengths. H. Küstner.—p. 2986.
Prevention of Conception and Moral Law. M. Hirsch.—p. 2992.
Unsuccessful Attempt at Hormonal Sterilization in a Man. M. Rodecurt. —p. 3004.
*Hormonal Sterilization of Female Mammals. A. Mandelstamm and W. K. Tschaikowsky.—p. 3004.
Bilateral Primary Carcinoma of Uterine Tubes. G. Haselhorst.—p. 3008.
*Psychic Influence on Female Genitalia. W. J. Zempléni.—p. 3012.
Therapy of Pruritus Vulvae. G. Siefart.—p. 3014.

Hormonal Sterilization of Female Mammals.—Mandelstamm and Tschaikowsky report that injections of 10 mouse units of prolan B (hormone of the anterior lobe of the hypophysis effecting luteinization) and even as much as 50 units are tolerated by white mice, without injurious effects. A single injection of prolan B produces temporary sterility in a large number of the animals. Of seventy-three mice, only eleven became pregnant during three estrual cycles. In mice that had been sterilized by hormonal treatment, a single injection of prolan prevented ovulation during five or six estrual cycles, and in some the sterility even lasted fifteen cycles. A repeated injection of 10 mouse units of prolan B effected sterility in all the examined animals (observation time of six mouse cycles). The authors conclude that injection of prolan B may prove to be helpful in inducing temporary sterilization of the female organism.

Psychic Influence on Female Genitalia.—In the introduction to his paper, Zempléni points out that the influence of the functional phases of the female genitalia (menarche, menstruation, pregnancy, labor, puerperium, lactation and menopause) on the psyche is generally recognized, for, in connection with those phases, serious psychic reactions and even psychoses have been observed. However, the influence of psychic factors on the genital functions is not so frequently recognized, yet two cases described by the author show that this is possible. In one case, premature menstruation set in as the result of apprehensiveness before a ball and thereafter always set in prematurely under the same conditions. The second case reported by the author concerns a woman who had an abortion as a result of a severe influenza during the tenth week of her first pregnancy. Because she had been told by her friends that all subsequent pregnancies would terminate during the tenth week, her apprehensiveness during the two following pregnancies actually had this effect, although there was apparently no cause for an abortion. During the next pregnancy her physician at first denied that she was pregnant and later this pregnancy was carried to term. The author also cites other conditions, such as war amenorrhea, which are probably due to psychic factors.

55: 3041-3104 (Oct. 17) 1931

*Reaction of Nongravid Human Uterus to Extracts of Posterior Lobe of Hypophysis. G. K. F. Schultze.—p. 3042.
Fetal Heart Sounds and Uterine Sounds on Phonograph Records. W. Rech and H. G. Clamann.—p. 3052.
Leukemia and Pregnancy. J. Saidl.—p. 3053.
Ligation of Veins in Puerperal Pyemia. A. Springer.—p. 3063.
Detrimental Results of Paragraph 218 Regarding Interruption of Pregnancy. M. Rodecurt.—p. 3069.
Influence of Physical Exercises on Female Organism During First Days of Puerperium. M. Merenitschewskaja.—p. 3071.

Reaction of Nongravid Human Uterus to Extracts of Posterior Lobe of Hypophysis.—Contrast roentgenoscopy of the uterus for diagnostic purposes gave Schultze the opportunity to make observations on its motor functions. However, he is convinced that the roentgenogram alone does not permit definite conclusions and that quantitative estimates should be based on the pressure registrations. If the reaction of the uterus following injection of extract from the posterior pituitary is determined by means of pressure registration, it is found that it corresponds to the menstrual cycle. At the beginning of the menstrual cycle the uterus reacts not at all or only slightly to the injection of extract of the posterior lobe of the hypophysis. About fourteen days after the menstruation, the contractions become stronger and of longer duration, and beginning with the twentieth day until twenty-four hours before menstruation sets in again the reaction capacity is very strong. Besides these observations on the dependence of the uterine reactivity on the ovarian cycle, the author made yet other observations on the course of the reaction. He found that in case

of intravenous application the action of the extracts sets in half a minute after completion of the injection. First there is a pressure decrease, which in turn is followed by a marked increase. The intensity of the reaction is likewise dependent on the dose. In estimations of the uterine contractions it is also significant to consider other factors that are of influence. There are "spontaneous" contractions caused by the contrast medium. The woman's excitement during the injection also causes strong contractions, and only after these have passed should the influence of the extract be estimated. The discharge of some of the contrast material and whether the tubes are open or closed is also of influence on the contractions. If large doses of the extract are injected there are certain unpleasant general reactions, such as a feeling of anxiety, severe headache, extreme paleness, enlargement of the pupils and retardation of the pulse. If small doses are given, the general reactions are slight.

Polska Gazeta Lekarska, Lwów

10: 829-844 (Oct. 25) 1931

The Three Internists of Krakow at Close of Nineteenth Century. L. Wachholtz.—p. 829.
*Function of Ovaries After Hysterectomy: Report on Animal Experimentation. K. Bochenski.—p. 832.
*Lymphadenoma and Amyloid Degeneration. J. Kostrzewski and Ciechanowski.—p. 834.
Relation Between Pituitary Body and Female Genital Organs. Seidler.—p. 838.

Function of Ovaries After Hysterectomy.—Bochenski divides the clinical symptoms ascribed to hysterectomy into two groups: those resulting from loss of the organ and those attending retrogressive degeneration of the ovaries. The first group embodies all local symptoms due to anatomic changes in the pelvis, plus removal of the internal secretion of the uterus; the occurrence of an internal secretion in the uterus is not, however, a generally accepted theory. Nine rabbits in which the uterus was removed and oophorectomy was performed six to twelve months later, did not show any macroscopic or microscopic changes in the ovaries as compared with control animals. The symptoms frequently encountered in women, and ascribed to hysterectomy, may be due to preexisting pathologic changes in the ovaries.

Lymphadenoma and Amyloid Degeneration (Hodgkin's Disease).—Kostrzewski and Ciechanowski discuss in detail this rare combination, of which only three cases are on record, two reported by Lichtwitz and one by Matthes. The case under discussion is of particular interest because of insignificant pseudoleukemic changes, general advanced amyloid degeneration and rare possibility of premortal diagnosis. The authors state that (1) the complication of lymphadenoma by amyloid degeneration is proved beyond doubt by this case; (2) there is no relation between the location or extent of the two diseases; (3) the presence of amyloid degeneration does not throw any light on the etiology of pseudoleukemia, and (4) the complication of lymphadenoma by amyloid changes proves that Hodgkin's disease is not a local disorder of the glandular system but a systemic disease with glandular symptoms.

Nederlandsch Tijdschrift voor Geneeskunde, Haarlem

75: 5191-5260 (Oct. 17) 1931

Idiosyncrasy Toward Cow's Milk. E. Gorter.—p. 5192.
*Transient Benign Coxitis. A. Colaco Belmonte.—p. 5197.
Plague Problem for Europe. J. J. Van Loghem.—p. 5200.
A Special Method for Making Roentgenograms of Cranium and Spinal Column. B. G. Ziedseus des Plantes.—p. 5218.
Hypoplasia Mandibulae with Attacks of Oppression. A. v. Westrienen and T. Jagerink.—p. 5223.
Atrophodermia Vermicularis. H. v. Voorneveld-Craciunescu.—p. 5226.

Transient Benign Coxitis.—Belmonte calls attention to a transient, benign infection of the hip joint, apparently little known in the Netherlands but frequently described in foreign journals. Coxitis fugax occurs chiefly in children and sometimes presents peculiarities that make early diagnosis possible. This is especially important for differentiation from tuberculous coxitis with a serious prognosis. Special treatment is not necessary. With rest in bed, the subjective and objective symptoms disappear after a few days or, at the most, a few weeks. The course is entirely favorable. A similar disorder occurs in the knee joint and there appears to be a similar spondylitis.

Bibliotek for Læger, Copenhagen

123: 381-436 (Sept.) 1931

*Cytologic and Metabolic Investigations on Excised Human Thyroids. M. Krogh, A. L. Lindberg and H. Okkels.—p. 381.
Occurrence of Diastase in Blood and Urine of Patients with Acute Infectious Diseases. Cont'd. K. Germer.—p. 403.

Investigations on Excised Human Thyroids.—Krogh and his associates find that cytologic examinations show exophthalmic goiter, unlike simple goiter, to be characterized by cellular hyperactivity, collapse of storage secretion, and proliferation. In patients treated preoperatively with iodine, the storage secretion is frequently restored but the morphologic signs of cellular hyperfunction, particularly the hypertrophy of the Golgi apparatus, are unchanged. The administration in adult male guinea-pigs of dried glands from simple goiters and from successfully treated exophthalmic goiters, in doses based on their iodine content, led to an increase in metabolism nearly equivalent to that caused by the administration of normal guinea-pig thyroids; glands from nontreated exophthalmic goiters and from unsuccessfully treated ones showed a biologic activity definitely below normal.

Svenska Läkaresällskapets Handlingar, Stockholm

57: 237-364, 1931

Some Points of View on Treatment, Especially Institutional Treatment of Neuroses. G. Kahlmeter.—p. 237.
Psychoanalysis and Natural Science. T. Lindner.—p. 246.
*Some Less Common Forms of Torsion of Adnexa. H. Marcus.—p. 249.
"Extra Dextrose" Eliminated After Intravenous and Oral Administration of Glycine to Phlorhizinized Dogs. F. Nord.—p. 274.
Effective Method of Hypnosis. G. Odencrantz.—p. 282.
*Spasmodic Torticollis and Operative Treatment. H. Olivecrona.—p. 284.
Importance of Making Certain Diagnosis in More Prolonged Mental Disorders Together with Danger of Private Care of Mental Disease Without Competent Medical Attention. A. Petrén.—p. 290.
Some Experiences with Active Psychotherapy. C. V. Söderlund.—p. 325.
Some Remarks on Muscular Sense. A. Tamm.—p. 327.
*Genuine and Postencephalitic Narcolepsy: Clinical Investigation. S. Wohlfahrt.—p. 342.
*Scorbutic Ménière's Symptom and Otosclerosis. H. Öhnell.—p. 358.

Some Less Common Forms of Torsion of Adnexa.—Marcus describes three cases of torsion of normal uterine appendages. In the first, in the third month of pregnancy, removal of the twisted adnexa did not affect the pregnancy, and normal delivery occurred at term. Excision was also done in the second case, and in the third the twisted adnexa were untwisted. Analogous cases from the literature are cited. The prognosis was good in all cases.

Spasmodic Torticollis and Operative Treatment.—Olivecrona reports six cases in which operative treatment resulted in marked improvement or in complete recovery. He states that recurrences are seldom to be feared and that, in cases of incomplete recovery, further improvement may be expected during the following years, probably because of the tendency of the condition to spontaneous recovery. He emphasizes that surgical division of the intraspinal portion of the accessory nerve should not be considered sufficient but that peripheral exeresis of the accessory nerve should as a rule be done. He advises against waiting for spontaneous recovery, as it usually takes years before the condition becomes somewhat endurable. When internal treatment, psychotherapy and so on are ineffective after six months, operative treatment is advocated. If, however, torticollis is only a partial phenomenon of some extrapyramidal syndrome, operative treatment is considered only in exceptional cases.

Genuine and Postencephalitic Narcolepsy.—Wohlfahrt reports four cases of true narcolepsy, all in younger men, two cases showing definite signs of disturbances of internal secretion closely resembling hypothyreosis. The administration of thyroid resulted in improvement. In three other cases reported, the symptoms are apparently related to a previous epidemic encephalitis.

Scorbutic Ménière's Symptom and Otosclerosis.—In Öhnell's case of Ménière's symptom in a patient with latent scurvy, the abundant administration of vitamin C resulted in marked improvement. The definite improvement in four other patients with Ménière's symptom after vitamin C had been given is believed to support the assumption that Ménière's symptom is in certain cases due to scurvy.